Report of The Yellow Fever Expedition to Yucatán, 1911-1912

(XXVIII Expedition of the Liverpool School of Tropical Medicine)

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BY

HARALD SEIDELIN

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REPORT OF YELLOW FEVER EXPEDITION TO YUCATAN, 1911-1912

(XXVIII Expedition of the Liverpool School of Tropical Medicine)

BY HARALD SEIDELIN.

When information had been received of the epidemic outbreak of yellow fever in Yucatán, in the autumn of 1911, the Liverpool School of Tropical Medicine resolved to send out an expedition with the object of carrying out further etiological researches, of which expedition I was put in charge.

The necessary arrangements having been made, I departed from Liverpool on December 9th, 1911, on the Cunard liner 'Lusitania,' arrived at New York on December 15th, and proceeded to Yucatán by the first available steamer, the Ward liner 'Esperanza,' on December 21st. I arrived at Progreso, December 29th, and at Mérida, the capital of Yucatán, the same day. I received much assistance from the Governor of Yucatán, Dr. N. Cámara, and from the Health Authorities and Hospital Physicians, and was at once given all facilities for starting work. My headquarters were arranged at the laboratory of the Hospital O'Horán, a very happy arrangement, since the Director, Dr. D. Hernandez, and staff of the laboratory gave me invaluable help in my work during the whole of my stay. The yellow fever lazaret is connected with the hospital, and I saw all patients in the lazaret with its Director, Dr. C. Vargas. I was also invited by Dr. F. Casares, Sanitary Delegate of the Superior Board of Health of Mexico, and by several practitioners, to see yellow fever cases and suspicious cases occurring in private practice. Post-mortem examinations were conducted at the hospital by Dr. H. Ayuso, or by myself. Experimental work was carried out at the laboratory or in the lazaret. Thus, I had ample opportunity of making use of the material available during my five months' stay in Yucatán, my observations being interrupted only by a mild attack of yellow fever which kept me from work for little more than a week. I sailed from Progreso on May 27th on the 'Esperanza' for New York, and landed at Liverpool on June 12th from the Cunard liner 'Campania.'

The principal object of the expedition was to study the relationship of *Paraplasma flavigenum* to yellow fever; besides that, I intended to make observations on other subjects if opportunity should present itself.

The report is divided into the following sections:—

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I. EPIDEMIOLOGY

The outbreak of yellow fever in Yucatán, of which I observed a part only, lasted from August 3rd, 1911, to April 30th, 1912. This period corresponds to the cases officially diagnosed as yellow fever. If several cases which, in all probability, belong to severe forms of yellow fever are included, the beginning of the outbreak must be dated from the last weeks of July, as is done by Lebredo (1911 and 1912) in his report, which deals with the earlier and more severe part of the outbreak, though he did not observe personally the first cases. This is the usual thing in yellow fever epidemics, that there is considerable doubt as to their actual beginning. The total number of cases officially diagnosed was 73, with 38 deaths.

The majority of cases—38—occurred in soldiers, Mexicans from various parts of the interior of the Republic, in which there is no yellow fever. Some additional cases can, perhaps, be traced to the same source of infection, namely, those occurring in soldiers' wives, who frequently visited the barracks, but did not live there. But several cases occurred, which had no connection whatever with soldiers or with soldiers' quarters, both in Mérida and in other towns, and in country districts. Yellow fever was officially reported from Kambul, Maxcanú, Temax, and S. Felipe, and I saw a case in Izamal, with Dr. Arzápalo, which in my opinion was yellow fever. Thus, it would be entirely unjustifiable to say that the outbreak had been limited to a certain class of the community, and with even less reason could it be said that it had been limited to a certain locality. The accompanying maps, of the city of Mérida and of Yucatán, illustrate the latter point.

During my earlier stay in Mérida, from 1906 to 1910, I had obtained no information of yellow fever cases occurring in the country districts; some earlier outbreaks were mentioned, but it was evident that their nature was not considered beyond dispute. Thus, I was inclined to regard Mérida as the only endemic focus of importance, though I was unable to explain why the inhabitants of the interior of Yucatán did not, as a rule, develop yellow fever when they stayed in Mérida, even if their first visit took place at a time when this disease was prevalent amongst foreigners. Isolated cases were reported in Indian boys who had come from some villages to the capital, but, on the whole, natives of country districts appeared to possess the same immunity as natives of Mérida. In 1911, García suggested (see Editorial, Bull. I, 6, pp. 199-201) that the outbreak in Mérida might have originated from cases infected in the territory of Quintana Roo. It was pointed out in the same editorial that there was no necessity of seeking the origin of an outbreak in Mérida, far away; importation had not been demonstrated, but there were amply sufficient reasons to regard Mérida as an endemically infected place.

My recent experience clearly shows that infection is not limited to Mérida, but this circumstance cannot, of course, alter my opinion that this capital must be looked upon as an endemic centre. It simply follows, that, in all probability, the whole of the State of Yucatán should be equally so considered. In the neighbouring State, Campeche, spontaneous cases have repeatedly occurred, and the Campechanos appear to enjoy the same immunity as the Yucatecos; according to this evidence, Campeche would appear to be equally infected. With regard to Quintana Roo, reliable information is difficult to obtain, but there is little doubt that autochtonous cases of yellow fever occur in that part of the peninsula also. It is, I believe, a well established fact, that yellow fever infection has been present, in a more or less active state, for years or probably for centuries, in the entire Yucatecan peninsula. No importation of virus has been necessary to keep up the infection, but the arrival of a considerable number of non-immune foreigners has, as a rule, been sufficient to give rise to a severe outbreak with typical cases, whilst, in the meantime, cases with less typical and less severe symptoms have occurred in natives. The last outbreak was caused by the arrival of two battalions of soldiers from non-infected parts of the Mexican Republic.

The view here taken is the same which I have advocated on several occasions, and is analogous to that which has been adopted by the large majority of observers. Marchoux (1908), Otto (1907), Boyce (1911), and many others are all of the same opinion, and the whole question of endemicity has recently been summed up in a very able manner by Simond (1912). With regard to the state of affairs in Yucatán, Lebredo (1911) expresses opinions very similar to my own. Objections to these views on endemicity are, however, still being raised, though mostly by authors without actual experience with yellow fever. It has been argued that all foreigners ought to contract the disease in endemic areas, if these were continually infected. It might just as well be said that measles is not endemic in most European capitals, because not every non-immune foreigner and every new-born child becomes infected. We know also that not all persons exposed to infection with yellow fever have become infected, not even in the most severe epidemics in previously non-infected countries; and we know quite well that some individuals in a plague-stricken house may escape infection, though all the occupants of the house would appear equally exposed to infection. In this case we cannot explain why, in one instance, one out of ten, and in another, four out of five, escape infection. We simply admit the fact and consider, as we ought to do in yellow fever also, that the transmission of a disease, and, perhaps, of an insect-borne disease more than of any other, is a complex affair. In the case of yellow fever, not all mosquitos are equally infected, not all individuals are bitten to the same extent, and, a factor which must be reckoned with in all diseases, not all individuals are equally susceptible to the infection. The yellow fever germ is not the cause of yellow fever in the sense that it, in all individuals and under all conditions, produces yellow fever, not any more than the mere presence of the tubercle bacillus produces tuberculosis. The presence of a pathogenic micro-organism is a necessary condition for the production of a certain disease, but another necessary condition is the susceptibility of the individual. This point has been fully proved by the results of experimental transmission of yellow fever. In the table of negative cases given by Carroll (1903) it is observed that in cases 12, 13, 15, 16, 17, 18, and 19, individuals were bitten by mosquitos after an interval of 12 days or more since these mosquitos had sucked blood from yellow fever patients during the first three days of the disease, that is, they were exposed to infection under conditions which must be considered highly favourable for the production of positive results. All these individuals were proved, by subsequent experiments, susceptible to infection with yellow fever. Other investigators have likewise failed to obtain positive results in all experiments. We cannot explain, with our present limited knowledge of the yellow fever germ, these facts, but we cannot deny them either. Thus, we know that a person may be exposed to infection with yellow fever without contracting the disease, and, if this happens in a high percentage of experimental cases, it is but reasonable to expect that it may happen more frequenty still under natural conditions. This occurs in all infectious diseases, and in most cases we can offer no other explanation than that of individual differences of susceptibility. In yellow fever we know something more. Not all persons who apparently escape yellow fever, do so because of lack of susceptibility or lack of opportunity of being bitten by infected mosquitos; in many it is a case of acquired immunity. Saint-Pair, in his notes published by Le Camus (1911), says that 'in an epidemic of yellow 'fever, the danger to which Europeans are exposed stands 'in inverse proportion to the length of their residence in the 'tropics'; the statement is illustrated by a table, from which I quote only, that of 200 soldiers who had been in the Colony (French Guiana) for 3 months, 27 per cent. died of yellow fever, but of 448 who had been there for 2 years, only 3 per cent. Equally illustrative examples can be found in many, especially older, works on yellow fever. This law is well known to physicians and residents in yellow fever countries, and would probably be accepted by all experienced observers if the words 'endemically infected areas' were substituted for 'the tropics.' The law, as all laws of a similar kind, admits exceptions, and the inverse proportion cannot, of course, be expected to be numerically exact, but generally speaking it will be found to hold good. Saint-Pair believed that foreigners lost their susceptibility when they got accustomed to their new surroundings, by which he probably meant to say that the (relative) immunity was due to climatic influences. We know now that this is not the case. I shall, later on, in the section on yellow fever in natives, give an illustration of the fact that climatic influences are of no importance.

There is evidently no other explanation possible than that of acquired immunity, which holds equally good in the case of foreigners of long residence, and in that of natives. When we consider this, we are forced to conclude that there must be an immense amount of mistaken diagnosis. Now, here is an important point. Lebredo (1911) holds that a diagnosis of yellow fever can always be made, in fact, he considers it a comparatively easy one when due attention is paid to the typical symptoms. Guiteras, in a discussion which I had with him and Lebredo in Habana, expressed the same opinion. This, of course, reflects seriously upon practitioners in yellow fever countries, but, even admitting that there is a general tendency not to diagnose yellow fever unless forced to do so, and also that a diagnosis can be made by more careful observation in a higher percentage of cases than is generally done, I fail entirely to see that the opinion referred to has any foundation in either practical experience or theoretical considerations. Experience shows us a gradually decreasing severity of yellow fever cases, from the rapidly fatal ones to others which end in recovery after a few days' illness with very mild symptoms. Then we know that some persons have been experimentally inoculated with yellow fever without contracting the disease, and that millions of people have possessed immunity to yellow fever without ever having suffered from it in anything like a typical form. If the yellow fever virus, when introduced into a human organism, can produce severe symptoms, mild symptoms, or no symptoms at all, nothing is more natural than that it can produce symptoms of so slight an intensity that it may become not only difficult, but even impossible, to recognize one or several of them. In no disease does a constant proportion exist between the intensity of various symptoms, nor is this the case in severe forms of yellow fever. How can it then be maintained that it should be so in the milder forms? I do not doubt that a man with Guiteras's vast experience can diagnose more cases of yellow fever than most other observers, but I feel sure, just as well, that a large number of cases would escape even his observation. In no disease can all cases be diagnosed by clinical observation alone. We have typhoid infections, malarial infections, plague infections, pneumococcus infections, scarlatina infections, and many others, without typical symptoms. In yellow fever I know of no symptom which is regarded, by several writers of authority, as a constant one. Not everybody who ingests cholera-vibrios contracts cholera: one presents no symptoms at all, but may become a microbe carrier; one presents a slight diarrhoea; one develops cholera in a typical, but mild form, and, finally, one dies from the infection. I know of no reason, why conditions should be different in yellow fever.

A very vexed question, but one which can be resolved by parasitological observation only, is this, whether there exist or not microbe carriers in yellow fever. I shall return to this question later on, but would at present consider it from an epidemiological point of view. There are many epidemiological facts, at present obscure, which would be easily explained, if the existence of microbe carriers were proved in yellow fever. The difficulty in explaining how intervals between outbreaks of yellow fever are bridged over, in sparsely populated areas, cannot be overlooked. The following quotation from Hudellet (1911), furnishes a good illustration of this difficulty.

'. . . it is very difficult to admit that the very scanty numbers of unfertilized, benumbed *Stegomyia* which persist, should be able to keep up the yellow fever virus from one winter to another, and to cause a "series of uninterrupted cases." It is also difficult to see how these *Stegomyia* could preserve the virus for many years in succession (1906-1910) without an epidemic outbreak being noticed.'

'It is much more reasonable to think that yellow fever infection exists in the Soudan in a form which is not known, but which is more resistant and less dependent on circumstances than the very fragile chain of conditions "*Stegomyia*—infected human organism—*Stegomyia*." It would be from this, at present unknown, source, that the infection would spread, when conditions became favourable, and *Stegomyia* numerous.'

It is more likely than anything else, that microbe carriers will be proved to constitute that unknown source to which Hudellet refers.

Another question of considerable epidemiological importance is that of reinfections. It has been, and is still, the common belief that yellow fever confers an absolute immunity, but in the literature many examples of reinfections are to be found, and their importance as an epidemiological factor is correctly emphasized by Simond (1912). I shall report, in the following section, a case of reinfection, and I have no doubt that it will soon be recognized that such cases are of quite common occurrence.

When the common occurrence of yellow fever in natives has been admitted, it remains to be considered, whether we are able to explain the striking fact that they seldom suffer from severe attacks. It would not be correct to say that fatal cases do not occur; in fact, yellow fever with all characteristic symptoms and fatal issue is occasionally observed in natives, both children and adults. There is, however, no comparison with the frequency of such cases amongst foreigners. We cannot speak here from actual knowledge, but two possibilities may be suggested. The experience of many observers tends to show, though it does not show it quite conclusively, that yellow fever, amongst foreigners, as a rule presents less severe and less typical characters in children than in adults. If this is true, we cannot be surprised that the same should be the case in natives. Most, or, in severely infected countries, practically all, natives will be exposed to infection in childhood, and, if reinfected later in life, will not be likely to develop severe attacks. The other possible explanation is that hereditary transmission of anti-bodies might take place; in this case native children would already possess a certain degree of immunity, and even their first case would probably be a mild one. The whole phenomenon is analogous to that observed in measles, which disease, as is well known, reveals a specially malignant character when introduced into a hitherto non-infected country. It might well happen that the pathogenic germ, when continually passing from one partially immunized human organism to another, would lose some of its virulence. If fresh material became available, the virulence would again increase gradually, just as various microbes acquire, experimentally, a higher degree of virulence when inoculated in series in highly susceptible animals. This corresponds to the observation which has often been made in yellow fever, that an outbreak begins with a series of mild cases, after which serious and fatal cases develop, and by and by increase in frequency. History of medicine shows that the characters of certain diseases, for instance, diphtheria and syphilis, undergo great changes from one epoch to another; also yellow fever has changed considerably. Its mortality may not be less nowadays than in earlier times, but the rapidly fatal cases with a general haemorrhagic tendency, which we meet with in older descriptions, are now very seldom seen.

We must not expect yellow fever to follow more rigorous laws than other infectious diseases, but should remain prepared to look out, not only for mild, but also for atypical cases, and make use of all means of arriving at a diagnosis, including microscopic examination of the blood.

I regard Mérida and other towns in Yucatán as endemic foci, and I shall continue to do so until they rid themselves from stegomyiae or reduce their numbers very considerably. As I have pointed out in a recent paper (1912), no other method of combating yellow fever can be relied upon in endemic areas. In the sparsely populated parts of the country the problem presents itself somewhat differently; the extermination of mosquitos is more difficult to attain, but, on the other hand, a less complete extermination is necessary. With less abundant human material available, it is likely that a not very considerable numerical decrease of the mosquito-hosts will cause the disease to die out.

An endemically infected area, as Yucatán, does not cease to be infected, because no cases are reported for several months—whether ten, or twenty, does not matter much. Even in much larger centres, as Habana, or Rio, in times of severe endemic infection, months or years have occurred in which no cases have been reported. Moreover, suspicious cases occur, even fatal cases, of which nothing is heard in the reports; Lebredo (1911) mentions such a case in a child, and I have been informed of several cases occurring in non-immune foreigners, in Mérida or other places in Yucatán, some ending fatally, others recovering, but all with symptoms extremely similar to those of yellow fever. For some reason or other they had not been submitted to an expert examination.

An anti-yellow fever campaign has been conducted in Mérida for several years, but up till now very little result has been obtained, as the last outbreak has clearly shown. There has been no reduction of mosquitos, and the house-to-house inspection has not given the expected result of tracing cases from their beginning; in fact, most cases have come under treatment on the third, or fourth, day, or later. A new plan of campaign has, however, recently been adopted by the President of the Superior Board of Health of the Mexican Republic, Dr. Licéaga, on the recommendation of his local delegate, Dr. Casares. A considerable increase of the number of medical and subordinate inspectors has been secured, and it is the intention to make a final effort to stamp out the infection. I have often discussed particulars of the matter with the health officials, and they quite agree to the overwhelming importance of the mosquito destruction measures, but at the same time feel convinced that they will be able to carry through an effective sanitary inspection of foreigners. Considering the local conditions, I very much doubt that the latter part of the programme will be practicable, but I trust that the eradication of mosquitos will be quite sufficient in itself to obtain the desired result. Together with the sanitation work in Mérida, a campaign should be started in the country districts, in which at present very little is done.

The extermination of yellow fever in Mérida will not only signify the disappearance of a very important focus of yellow fever, but will also give a strong impulse to other places which still lag behind in their sanitary measures.

In the appendix a table is given of all the cases which have been officially diagnosed during the outbreak in Mérida, and documents connected with the anti-yellow fever campaign in that place.

II. CASES OBSERVED

From my arrival until I left Mérida—that is, during the first five months of 1912—twenty-three cases were officially diagnosed as yellow fever. In six cases, which were not seen by me, a retrospective diagnosis was made; they had all occurred in native Indians. One case, which was also that of a native, I did not observe clinically, but performed a post-mortem examination, on which occasion the diagnosis was made. I have in an earlier paper (1911, 3) discussed the clinical aspect of yellow fever in Yucatán, and Lebredo (1911) has recently given a detailed account of a a number of cases observed in Mérida. I shall therefore not give full particulars of the remaining seventeen cases which I observed clinically, but only make use of my notes from a few cases to illustrate some particular features.

The following is a fatal case in which the fall of temperature and increase of pulse rate, towards death, are well marked. There is a slight remission of the temperature on the fifth day; the patient was not under observation at a time, when a deeper remission would have been likely to have taken place.

F.O., 27 years, female, native of Jocona, Mexico (Chart I).—Patient is unable to give a clear account of her illness, but believes, when entering lazaret, on *January* 2, that she has been ill for some ten or twelve days. Dr. Dussart, however, who saw patient on December 30, in Temax, is of opinion that this was the first or second day of her illness. She walks without help into the lazaret.

Patient complains now of headache, and pain in the back and lower extremities.

There is conjunctival hyperaemia and slight conjunctival jaundice. Nausea. Tongue coated, with red borders. Pulse strong and full.

January 3.—No pain. Hyperaemia of conjunctivae less pronounced. No epigastric pain, not even on pressure. Liver and spleen not enlarged. Tongue as yesterday. Gums swollen and hyperaemic. Black vomit. Pulse soft, heart dulness normal. Feels subjectively well.

January 4.—Slight general jaundice.

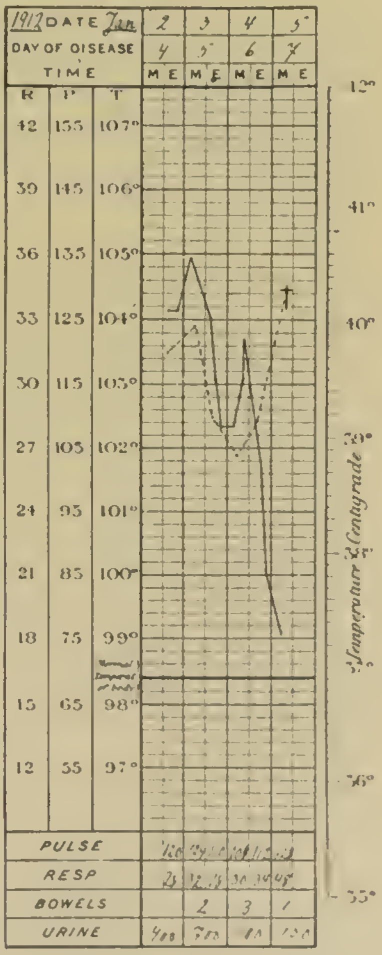


Chart I

The blood contained *Paraplasma flavigenum*, but no malarial parasites.

Urine, January 3: cloudy, sp. gr. 1·020, acid, 2·5 ‰ albumin, indican reaction faintly positive, bile pigment and urobilin present, diazo reaction positive, numerous hyaline and granular casts, numerous leucocytes, no erythrocytes, few renal epithelia, numerous duct epithelia.

January 4: 3 ‰ albumin, bile pigment in considerable quantity diazo reaction faintly positive.

Death took place in the early morning of the fifth of January, which was probably the seventh day of the disease.

Abstract of post-mortem examination (by Dr. Ayuso), at 9 o'clock in the morning, six hours after death: Universal jaundice.

Cephalo-rachidial cavity: Meningeal hyperaemia.

Thoracic cavity: Pericardium hyperaemic, with small ecchymoses, contains a small quantity of yellow fluid. Myocardium soft and yellowish. Slight sero-fibrinous pleuritis, and congestive foci in the lungs.

Abdominal cavity: Liver, 1,020 gs., of reduced size and diminished consistence. Colour intensely yellow, with red dots corresponding to dilated blood-vessels. Spleen, 240 gs., with fibrous capsule thickened and pulp softened, friable. Kidneys, 150 gs. each, congested, with alternating red and yellowish portions. The stomach presents small ecchymoses and ulcerations in its mucous membrane, and contains about 300 c.c. of dark, blood-stained fluid. Intestines also somewhat congested, with ecchymoses and a small quantity of thick, black fluid.

This case was officially diagnosed as yellow fever on January 4th.

I shall now give the notes of a mild case, ending in recovery:—

M.G., 21 years, female, Mexican (Chart II).

This patient belonged to a religious sisterhood, and was ill in their house in Maxcanú. I saw her on January 5th, together with Drs. Casares, Dominguez, Dussart, and Hernandez. I am indebted to Dr. Dominguez for the notes from the days previous to the fifth.

Patient had been in Mérida for a few days a short time ago, and returned to Maxcanú on December 22nd. There has been yellow fever in Maxcanú on several occasions, and the inhabitants are considered immune; thus, there seems to be no reason why the infection should not have been contracted in Maxcanú. Patient has lived one year in Yucatán.

December 31, 1911.—Feels slightly unwell.

January 1, 1912.—Headache, and pains in the whole body, mostly in the loins.

January 2.—Pains continue, especially in the epigastrium.

January 3.—Bilious and watery vomits.

January 5.—Slight conjunctival injection, tongue clean, with intensely red borders and tip; also gums very red. There is a slight temperature rise in the evening after our visit; patient is very nervous and upset, believing that the visit of so many doctors indicates that she is in a very serious state.

January 6.—Slight jaundice of conjunctivae.

In the *blood* the *Paraplasma flavigenum* was found, but no malarial parasites.

The *urine* has been very scanty, especially during the second, third and fourth days. When examined, on January 5, it was found to contain a trace of albumin and a few granular casts, but no bile pigment.

Recovery

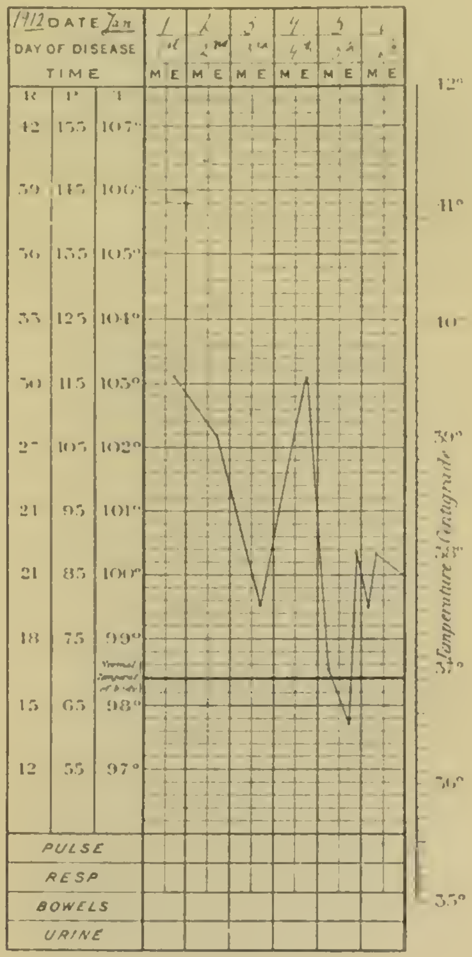


CHART II

The official diagnosis of yellow fever was made on January 5th.

In several mild cases no official diagnosis of yellow fever was made, but to my mind the clinical symptoms, even without considering the examination of the blood, leave little doubt as to the nature of the cases. The following are examples of this type of case.

F.P., 30 years, male, Spanish (Chart III).

January 8, 1912.—Cephalalgia, rachialgia, pains in lower limbs. Cold sweating. Tongue coated, with red borders. Foetor ex ore. Slight jaundice of conjunctivae. Resp. normal. Pulse strong.

January 9.—Less pain. Slight increase of jaundice. Pulse normal. 700 c.c. of urine, containing a trace of albumin.

January 10.—No pain. Jaundice as yesterday. The urine contains a trace of albumin, casts, and a few renal epithelia. Indican reaction intensely positive, diazo reaction negative. Numerous calcium oxalate crystals.

January 11.—Feels well.

January 12.—Jaundice almost disappeared.

On January 15 no albumin was found in the urine, but on January 17, when F.P. was about at his work, a faint trace of albumin. On one or two occasions later on the urine was examined, no albumin being present.

The *blood* contained *Paraplasma flavigenum*, but no malarial parasites.

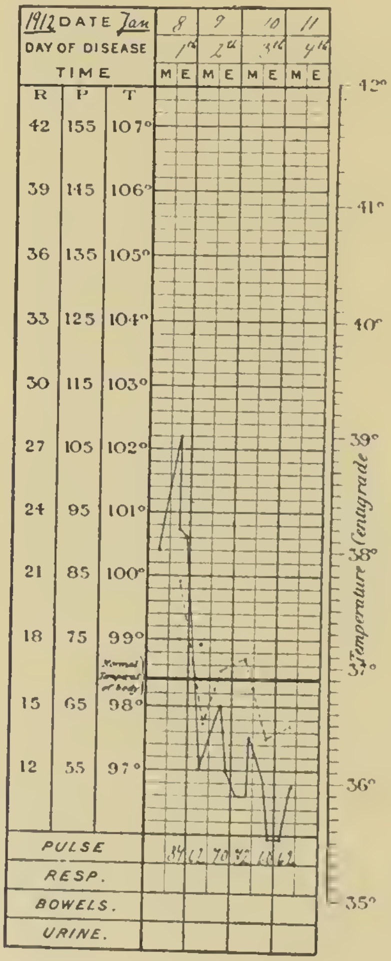


Chart III

An official diagnosis of gastric fever was made in this case, but my diagnosis was yellow fever.

R.B., 22 years, male, Mexican (from non-infected part of the Republic) (Chart IV).

January 11, 1912.—Headache and pains in back and loins, also in epigastrium. Weakness of limbs. Slight conjunctival jaundice. Tongue coated, with fissures in central portion, and red borders.

January 12.—Jaundice persists, but other symptoms have disappeared.

The blood contained *Paraplasma flavigenum*, but no malarial parasites.

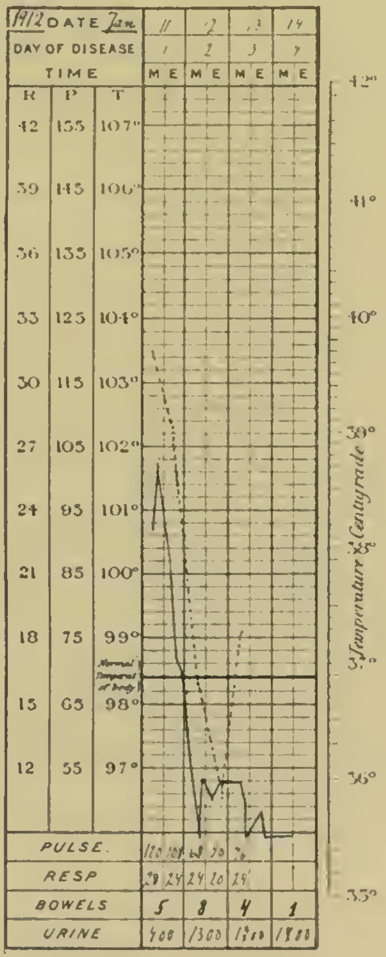


Chart IV

The official diagnosis in this case was 'embarazo gastrico' (embarras gastrique), my diagnosis being yellow fever.

M.R., 20 years, male, Mexican (from Hermosillo, in the State of Sonora, in which there is no yellow fever). Has lived five years in Yucatán (Chart V).

February 24, 1912.—From yesterday general ill-feeling, headache, backache, and nausea.

There is jaundice and hyperaemia of sclerae; the tongue is coated, with red borders and tip. Epigastric pains.

February 25.—Symptoms increasing. Jaundice also of the face.

February 26.—Feels better.

From *February* 27 patient gradually improved, and made an uninterrupted recovery.

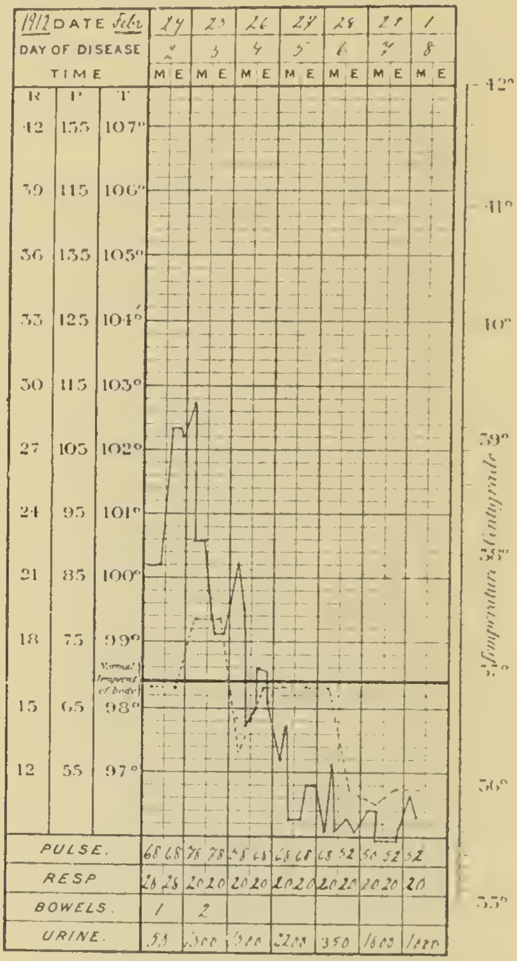


Chart V

Examination of the *blood* showed, on February 26, the presence of *Paraplasma flavigenum*, and absence of malarial parasites.

The urine contained albumin in small quantity.

This case was officially diagnosed as bilious fever, but my diagnosis was yellow fever.

L.M., 32 years, male, Mexican (Hermosillo, Sonora). Has lived four years in Yucatán (Chart VI).

March 16, 1912.—First day of illness. Slight headache and epigastralgia. Tongue coated, with red borders. Photophobia. Hyperaemia of conjunctivae and jaundice of sclerae.

March 17.—Less headache. No epigastric pain.

March 18.—No headache. Jaundice unaltered.

March 20.—Jaundice less.

March 21.—Complete recovery.

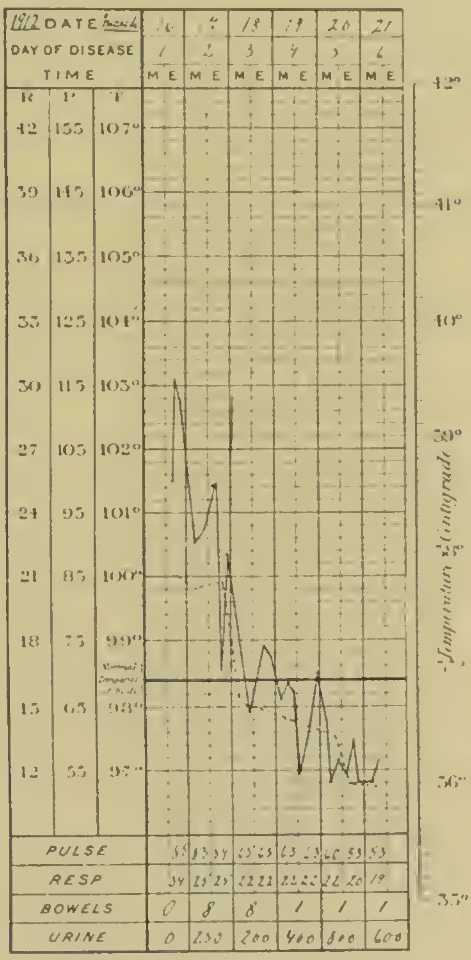


CHART VI

The *blood* contained, on March 16, *Paraplasma flavigenum*, but not on March 18. *Plasmodium* absent.

Urine. March 17: acid, contains albumin (traces) and a few granular casts, numerous renal epithelia, and polymorphonuclear leucocytes. The diazo reaction is positive, and the indican reaction intensely so, but reactions for bile pigments and urobilin are negative.

March 20: 0·40 °/₀₀ albumin. Numerous granular casts, few renal cells and polymorphonuclear leucocytes. Indican reaction and reaction for urobilin intensely positive, reaction for bile pigments faintly positive, and diazo reaction negative.

This case was both officially and by myself diagnosed as yellow fever.

It is remarkable that *Paraplasma flavigenum* was found on the first day of disease only, but it should be mentioned that it was not found possible to make repeated examinations of the blood during convalescence.

H.S., 33 years, male, Dane (Chart VII).

March 29, 1912.—In the evening headache and lassitude.

March 30.—Febrile symptoms, headache, rachialgia, chiefly lumbar, and pains in extremities. Urine contains no albumin.

March 31.—Slight headache in the morning. Unable to work as usual; very tired in the afternoon. Urine contains a trace of albumin and some casts, gives a strong reaction of urobilin.

April 1.—Headache, chiefly frontal. General ill-feeling. Pains in extremities. Stays in bed.

April 2.—Slight jaundice and considerable lassitude.

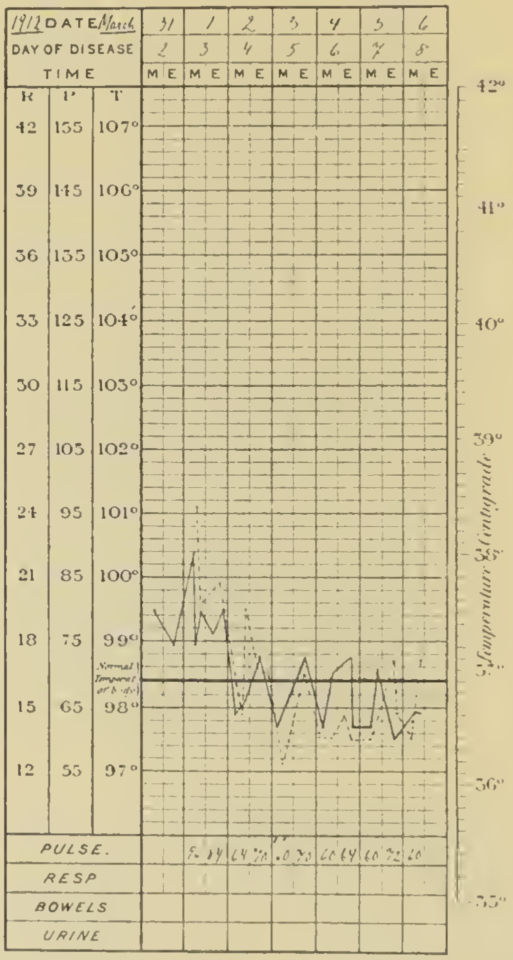


Chart VII

Examination of *blood* shows the presence of *Paraplasma flavigenum* on March 30 & 31, and April 1, 4 & 8, but not on April 12, and not on various occasions later than this date. Malarial parasites were absent.

The *urine* was abundant during the whole time; large quantities of fluids were taken systematically. Albumin was present in small quantities, traces, or, at any rate, not estimable. Albuminuria continued for some time after the disappearance of other symptoms, and was observed for the last time on April 16th; after that time albumin was never found, though the urine was carefully tested almost daily for several weeks. Hyaline and granular casts were occasionally found even after the disappearance of albumin. A small number of leucocytes were frequently present. A few erythrocytes were found once, when calcium oxalate crystals, which were of common occurrence during convalescence, were particularly abundant. Indican was often demonstrated. Urobilin was found during the illness in considerable amount, and, later on, occasionally in small quantity. Bilirubin was never found, and diazo reaction was negative throughout.

In this, my own, case I discussed the diagnosis with Drs. Palomeque and Hernandez, who saw me during my illness. Dr. Palomeque, who has a very large experience, believed, to begin with, that the case was one of malarial infection, but the absence of malarial parasites and the prompt recovery without the administration of quinine made him abandon that idea. After having followed the course of the disease, he felt very much inclined to adopt the diagnosis of yellow fever, which I had made from the onset, after having found the *Paraplasma flavigenum*; but, on accepting this diagnosis, he declared it as his conviction that my earlier case, five and a half years ago, which he had not observed, had not been one of yellow fever. Dr. Hernandez was quite satisfied that yellow fever was the correct diagnosis. Officially no diagnosis was made, but the case was generally spoken of as one of 'surménage.'

The presence of jaundice and albuminuria, and the low pulse rate, in a mild case of acute febrile disease, occurring in an individual exposed to yellow fever infection, make it, as far as I can see, extremely probable that the disease was really of this nature. The intense headache, general ill-feeling, and considerable loss of strength, were also characteristic. The circumstance that this probably was my second attack of yellow fever, constitutes no objection to accepting that diagnosis. Various authors, especially Marchoux and Simond (1906) regard the repetition of yellow fever in an individual as quite a common occurrence. Durham (1911) also believes he has experienced personally a second infection. My earlier case, the chart of which is given in my paper on diagnosis (1911, 3), was, in all probability, one of yellow fever, and this I regard as the explanation, why my present attack was so very mild. On the other hand, it must be admitted that such a mild case would be very likely, in any epidemic, to escape detection; hence the very great epidemiological importance of such cases.

I do not intend to discuss, in this place, diagnosis in general, but I would like to make a few remarks on some of the more important symptoms and their significance.

It is recognized by most observers that black vomit is very far from being a constant symptom; thus, it is not surprising that it is often absent in our cases.

Jaundice has been a constant symptom in this series of cases, but it should not be taken for granted that it is always so. Observers with very large experience, as Azevedo Sodré and Couto (1901), have found it absent in some cases, even after death.

Bile pigments were found frequently, but not constantly, in the urine.

Albuminuria has also been found in all those of our cases in which the urine has been examined. I regard this as one of the most constant symptoms, but, as we find the quantity of albumin varying from ten grammes or more in the litre to the faintest possible trace, corresponding to all degrees of intensity of the kidney affection, there seems to be no reason why it should not occasionally be absent altogether.

Ehrlich's diazo reaction was positive in three cases in this series. This is a comparatively high percentage, as careful examination of the urine could be made in eleven cases only, and in very few of these from the beginning of the disease. There is, of course, no possibility of error in such a simple test as the diazo reaction, when the prescribed technique is followed carefully. The urinary analyses were made by Lic. A. Villa, who is in charge of the chemical laboratory and has a large experience, and all positive diazo reactions, both in this and in my earlier series of cases, were seen by myself.

A low pulse rate is present during the latter part of the disease, or, at any rate, in convalescence, in probably all uncomplicated cases, but the extent to which it decreases, varies considerably.

The following case was of great interest to me, as it was the first in my experience which was complicated with parotitis. This complication is said by Azevedo Sodré and

Couto (1901) and Thomas (1910) to be of not uncommon occurrence in Brazil, whilst it is seldom observed elsewhere. The surgeon who performed the operation on this patient stated that this was the third case he had seen in yellow fever, and several colleagues who had practised in Yucatán for many years had never seen this complication, and considered its presence as almost excluding the diagnosis of yellow fever.

In this case the temperature and pulse curves were on the decline, but were interrupted by the complication which produced secondary rises.

I.A., 20 years, male, Mexican (from Pachuca, yellow fever free place). Chart VIII.

December 30, 1911.—Entered lazaret in a subdelirious state, and was unable to give a definite history of his disease or previous movements. The following notes were supplied by Dr. Dussart, Chief Medical Officer of the 'Cruz Blanca Mexicana':—I.A., a private soldier, arrived in Yucatán on December 18, 1911, at Espita December 19, and at Temax December 20, from which place he was sent out in detachment with other soldiers, being in Tzilán on December 22, and returned to Temax on the 26th. He was taken ill on December 27, and was sent to the lazaret on the 30th, the following observations having been made in Temax the same morning: Tp. 39·6° C., conjunctivae inflamed, tongue coated; cephalalgia, rachialgia, and epigastralgia.

After his arrival, patient complained of cephalalgia and intense epigastric pain. There was foetor ex ore, the tongue was coated, gums haemorrhagic, eyes injected, slight jaundice.

December 31: Pains in the whole body, most pronounced in the back. Pain in epigastrium, on pressure. Liver slightly enlarged and slightly tender. Delirium.

January 1, 1912.—Epigastric pain less pronounced. Right parotid gland slightly enlarged.

January 2.—Patient continues delirious.

January 3.—Delirium less pronounced. Right parotid gland considerably, left slightly, enlarged.

January 4.—General improvement. Eyes but slightly injected. Parotid glands painful. Light jaundice.

After this date improvement of the general state continues, but the enlargement of the parotid gland on either side increases, and patient is transferred to a surgical department, where incisions are made by Dr. S. Guzman a few days later, and pus evacuated. Afterwards recovery was uninterrupted, and patient left hospital January 27th.

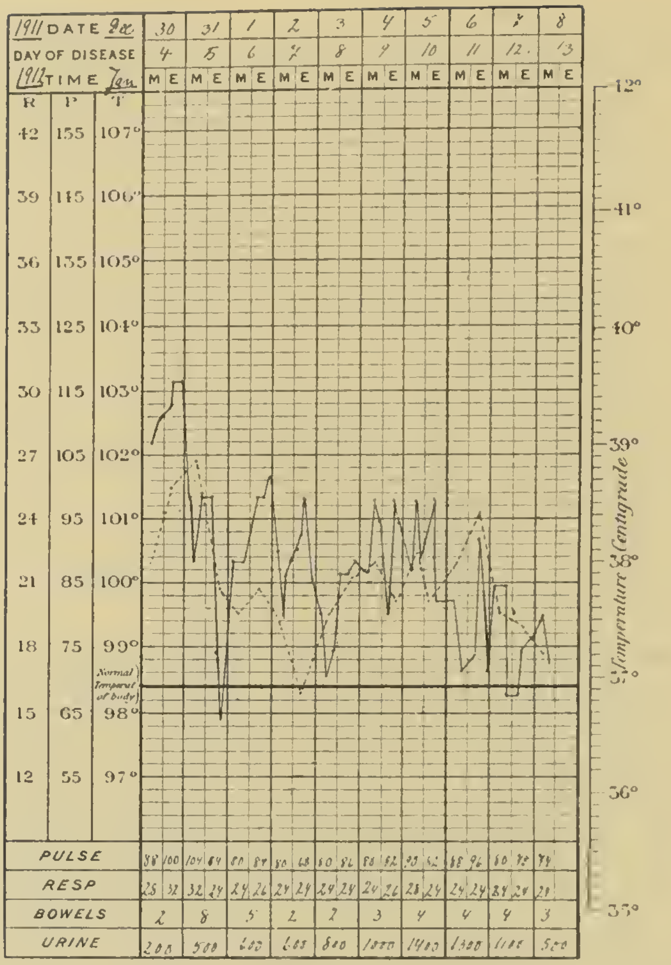


Chart VIII.

In the *blood Paraplasma flavigenum* was found, but no malarial parasites.

Urine, December 31, 1911 : Reaction, acid, sp. gr. 1·010, albumin 0·75 $^{\circ}/_{\circ\circ}$, indican reaction faintly positive, diazo reaction negative. There is a considerable amount of urobilin, but no bile pigments ; no haemoglobin. Numerous granular casts, numerous cylindroids, few polymorphonuclear leucocytes ; no erythrocytes. Few renal cells, many urinary duct cells.

In this patient the hygienic conditions of the mouth were very bad, but the same has been the case in many other patients observed in this and in earlier outbreaks.

Parotitis in yellow fever is probably no specific lesion, but simply the result of a canalicular infection with pyogenic microbes, ascending from the mouth, and favoured by the lowered resistance of the individual. If this is true, it is only surprising that parotitis is not a more frequent complication.

In another case—in an old man—yellow fever infection was apparently disappearing when the already existing symptoms of nephritis increased, and the pulse rate, which had fallen below 60, again began to increase. The temperature rose in a single day from below normal to 104° F. (40° C.), symptoms of pneumonia developed, and patient, who was apparently on his way to recovery, rapidly lost ground. Death ensued a few days later. I insert a brief summary of this case, which was not seen until about the sixth day of disease.

P.T., 64 years, Mexican (México City). (Chart IX.)

February 21, 1912.—Intense headache and backache; epigastric pain, increasing on pressure. Conjunctival hyperaemia and light scleral jaundice.

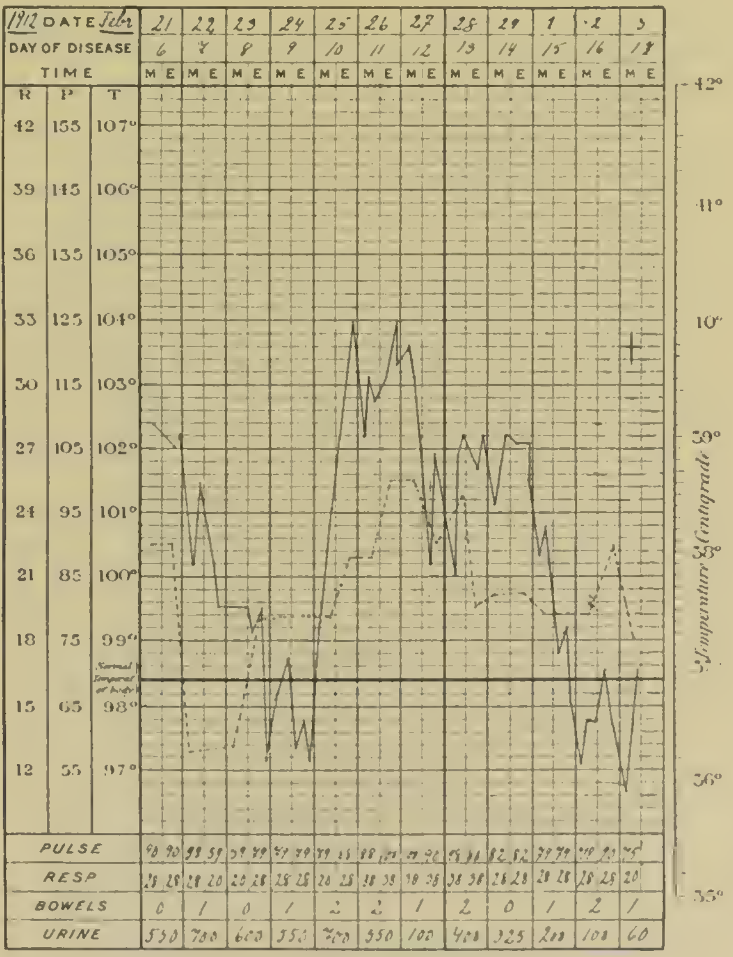


CHART IX.

February 23.—Pains persist. Albumin constantly present in urine, the amount increasing. During the following days patient gradually lost strength, and died on March 3.

The *blood* contained *Paraplasma flavigenum*, but no malarial parasites.

The *urine* contained up to 2 °/₀₀ albumin, numerous hyaline and granular casts, numerous leucocytes, and a few renal epithelia; it contained small amounts of indican and bile-pigments; diazo reaction negative.

At *post-mortem* examination haemorrhagic gastritis and enteritis were found, and advanced fatty metamorphosis of the liver. The upper lobe of the right lung was in a state of grey hepatisation, and the remaining parts of the lungs congested. There was intense parenchymatous nephritis, and some sero-fibrinous pericarditis; the spleen was considerably enlarged.

In the following case the rise of temperature was of very short duration, and, as far as observed—patient was seen on second day of disease—very slight. In comparison with this mild febrile reaction, other symptoms were more pronounced than one would have expected, jaundice being visible not only in the scleral conjunctivae, but also in the skin, and lasting, as well as albuminuria, for about a week.

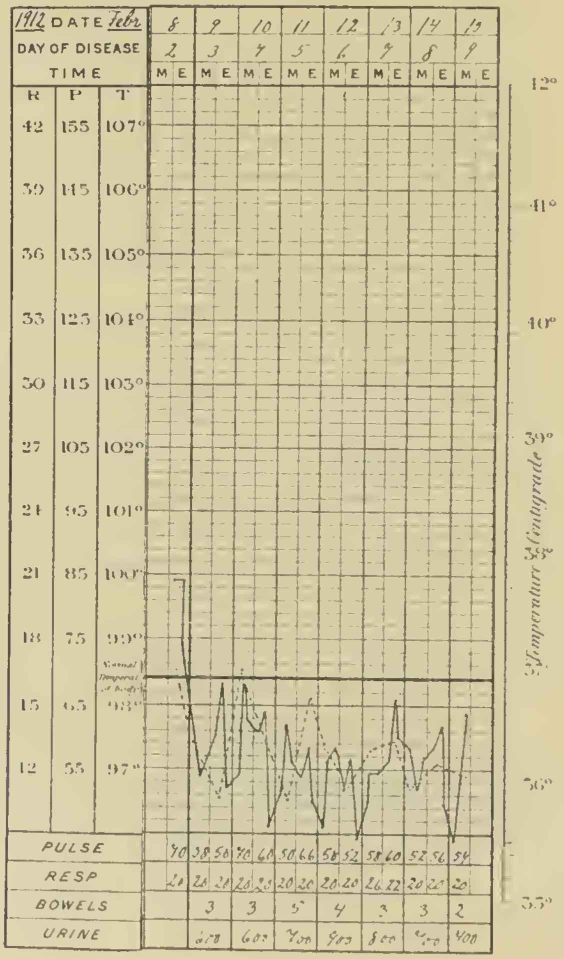


Chart X.

L.P., 26 years, male, Mexican (Oaxaca, a yellow fever free place). (Chart X.)

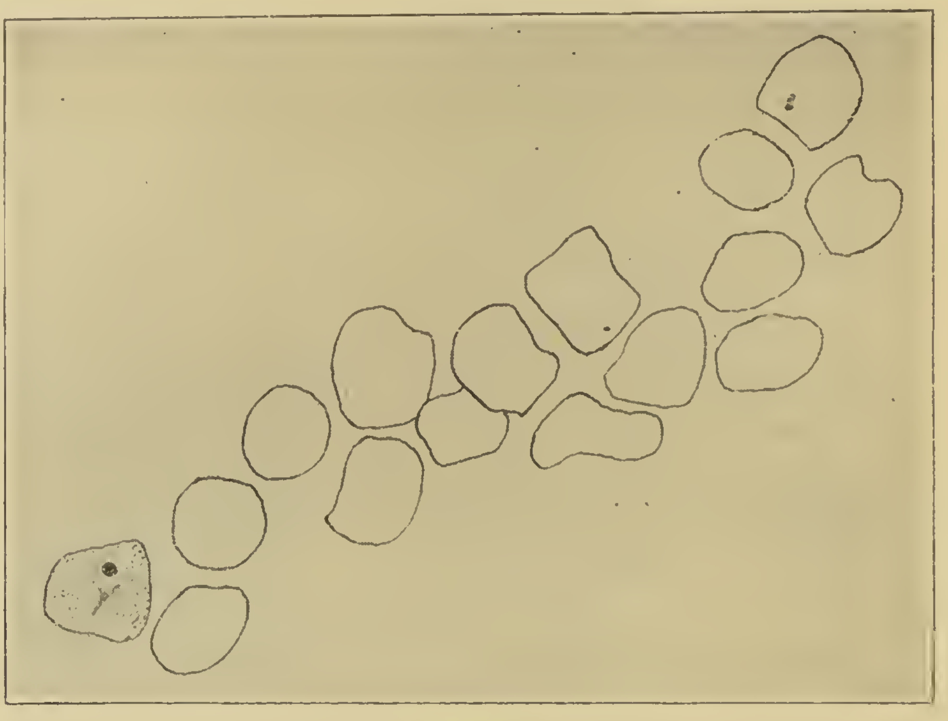
February 8, 1912.—Patient enters lazaret on second day of disease, complaining of headache, principally frontal, rachialgia and intense pain in the loins, slight epigastralgia. Jaundice visible in face, and more intense in sclerae. Slight conjunctival hyperaemia. Tongue coated, with red borders. Nausea.

February 9.—Slight improvement of symptoms, but pain in loins still intense. From this date symptoms vanished slowly. Patient made a complete recovery and left hospital *February* 15.

In the *blood Paraplasma flavigenum* was found, but no malarial parasites.

The *urine* contained no albumin on February 8, but small quantities from February 10 onwards; but not on February 15. Numerous hyaline casts and polymorphonuclear leucocytes; no erythrocytes; few renal cells. No haemoglobin, no bile pigments. Diazo reaction negative.

A considerable number of malarial cases were observed, at the time of the yellow fever outbreak, and were sent to the lazaret, in compliance with the law, which prescribes that all non-immune foreigners, when presenting a rise of temperature, shall be regarded as suspicious of yellow fever until the contrary be proved. In no case, however, in the lazaret was yellow fever found together with malaria, but this coincidence was observed in a patient whom I saw in a private house with Dr. J. Patrón, by invitation. This patient was a French lady, who had lived in Mérida a few months. She had no previous history of malaria, and had visited no notoriously malaria-infected places in Yucatán. She was taken acutely ill with fever, vomiting, but no black vomit, and jaundice. Dr. Patrón regarded the case as a moderately severe attack of yellow fever, but after a few days the temperature became intermittent, and an examination of the blood was suggested. Before the result of this was known, Dr. Patrón mentioned to the family with whom patient lived that the disease might be a mixed infection with malaria and yellow fever, and this diagnosis was officially accepted. It quite agreed also with the result of the blood examination which showed the presence of *Paraplasma flavigenum* and *Plasmodium vivax*. Quinine was given, and patient recovered after a rather severe illness of about a week's duration. The source of her malarial infection was never discovered; in the house only *Stegomyia* larvae were found, but it was situated in one of the outskirts of the city, and patient used to walk about the suburbs in the late afternoon. The following sketch shows part of a microscopic field of a blood-specimen from this patient.



Text Fig. I.

Several additional clinical observations, presenting features of interest, will be found in the sections on 'yellow fever in natives' and on 'treatment.'

III. YELLOW FEVER IN NATIVES

I

Natives in endemic areas are considered immune to yellow fever. This statement is agreed to by medical practitioners, and in the literature it is either expressly put forward or tacitly accepted. Many authors, especially in earlier times, take it simply for granted that this immunity is due to climatic influence, and do not consider the phenomenon worth much discussion. Even comparatively recent authors, as Azevedo Sodré and Couto (1901), whilst admitting that the occurrence of mild cases among the natives may play a secondary rôle, are of opinion that climate is the principal factor in establishing their immunity.

In most modern treatises on yellow fever, however, the former factor is considered the only one responsible for the immunity; thus, especially in those by Otto (1907), by Boyce (1911), and by Clarac and Simond (1912).

The complete change of opinion which has taken place depends more on general considerations, to a large extent of an epidemiological nature, than on personal observations. As a matter of fact, few actual observations of yellow fever cases in natives have been published.

Some cases have been reported from Brazil by Marchoux and Simond (1906), and from the West Coast of Africa by Boyce (1911); Guiteras (1902) has reported cases in native children in Cuba. Several authors have reported isolated cases.

No special study has been made of this form of the disease, based on a large amount of material. Such a study, however, would be of very considerable interest, as it might be possible to find out the special characters of the disease in more or less immunized individuals. It is said in general terms that yellow fever assumes a less severe form in natives than in foreigners, but further particulars are not known.

It may, therefore, be of some interest to make known the following reports which I have been able to collect in an endemic locality. For most of the reports I am indebted to colleagues, as I have observed personally only a few of these cases. The notes should be considered in the light of a contribution to the subject only, the reports not being sufficiently detailed to attempt a complete study.

2

In Yucatán, as elsewhere in endemic centres, the natives are, in general medical practice, considered immune to yellow fever. When a native is taken ill with fever, no diagnosis of yellow fever is considered, whilst, in the case of a foreigner, the medical attendant is under legal obligation to consider, first of all, this diagnosis. If, however, the matter is brought under discussion, it is soon found out that a large number of local physicians are acquainted with one or more cases of yellow fever in Creoles or in native Indians, either from their own practice, or from that of their friends. Through the kindness of numerous colleagues I have been able to collect reports of a considerable number of cases, not hitherto published, which may conveniently be preceded by a brief resumé of the publications on the same subject which have appeared in Yucatán.

The earliest paper which has come to my knowledge is one by Carrillo (1892), Bishop of Yucatán. This author deals with the question from a historical point of view, and finds evidence, in old Indian documents, of the existence of yellow fever amongst the natives before the discovery of the country by the Spanish. The author refers to statements which seem to show that yellow fever was not then an endemic disease of Yucatán, but manifested itself in epidemic outbreaks. A definite conclusion can, however, not be drawn from the very brief descriptions quoted, especially when considering that epidemic outbreaks have been observed repeatedly in modern times also, during which Yucatán has, quite correctly, been looked upon as an endemic area.

According to Molina (1910) outbreaks of yellow fever, with more or less pronounced epidemic characters, have occurred in Yucatán in the years of 1527, 1648-50, 1662, 1699, 1715, 1802, and 1825. Mr. Molina, in conversation, informed me that it was not quite clear, whether the outbreak in 1527 was really one of yellow fever, and, also, that in most outbreaks it is not clear, whether natives were attacked, or not. In the report of the epidemic of 1648-50 it is, however, stated that Spaniards, Creoles, Indians, Negroes, and Mulattos died. And the epidemic of 1715 is said to have occurred amongst foreigners and natives.

Two papers, by Canton and by Pompeyo, deal with an outbreak which took place in Dzitás during the months from July to October, 1903. Numerous cases were observed, to begin with in foreigners, but later on in natives also.

Not all the physicians who observed the cases concurred in the diagnosis of yellow fever, but, according to the symptoms described by Canton in his paper, and verbally to me by Dr. Pompeyo, there can be no reasonable doubt as to the correctness of this diagnosis. Canton (1906) mentions the following symptoms:—Conjunctival injection, epigastric anxiety, bilious vomit to begin with, afterwards typical black vomit, temperatures up to and above 40° C., albuminuria, hiccough, and jaundice. There was no intermittency, and quinine was without effect, whilst many cases, being treated with purgatives only, recovered without either recrudescence or relapse. The author discusses the question of immunity, being of opinion that the reason why he and the other physicians present remained unattacked by the disease was that they were inhabitants of Mérida, where yellow fever is endemic, thus clearly establishing a difference between the capital of Yucatán and the country districts.

Pompeyo (1909), in his paper, does not enter into a detailed discussion, but expresses his firm conviction that the epidemic disease in Dzitás in 1903 was genuine yellow fever, as diagnosed by Dr. Cardenas, the first physician commissioned by the Government to report on the epidemic. This author mentions that, according to tradition, there was in the years 1825 to 1830 an epidemic outbreak of fever, the nature of which was unknown, but which terminated with abundant cases of blood vomiting. Pompeyo has also obtained information of outbreaks in Calkini and Calcehtok, in the years of 1877 and 1878. These evidently occurred principally in natives.

Official reports of the epidemic in Dzitás, by Drs. Cardenas and Canton, were published in the 'Diario Oficial,' Mérida, 1903. From these reports it appears evident—and the conclusion was drawn by the authors—that the outbreak was one of yellow fever, though with an exceptionally low mortality. Dr. Cardenas saw 74 cases, and, at the time of his report, 40 had recovered and only 4 died.

3

I shall now give a summary of the information which I have received from physicians in Yucatán. As will be seen, a large number of colleagues have with great readiness and amiability responded to my inquiries, but the data collected cannot, by any means, be considered complete; I do not believe they include, even approximately, all cases which have occurred in later years with symptoms sufficiently characteristic to make a medical diagnosis possible. No systematic enquiry has been made, but private inquiries only, as the opportunity presented itself. It must, moreover, always be kept in mind that to the reluctance against making a diagnosis of yellow fever which generally obtains, is added an often almost invincible incredulousness in the minds of many medical men when the cases in natives of endemic areas are under discussion.

Dr. F. Losa has observed an outbreak of typical yellow fever in natives, Creoles, and Indians, which took place during the year from summer 1878 to summer 1879, in Tizimín. This little town (see map) is at a distance of 160 kms. from Mérida. It is not even now connected with Mérida by railway, and in 1878 not only part, but the whole distance to the capital had to be covered in carriage. It may be presumed that the difficult means of transport would render the transmission of a disease, of the nature of yellow fever, less easy also.

Tizimín is divided in two parts, one being situated on a slightly higher level than the other, the difference being about 2 metres. The lower part is the larger one. Most poor people live in the higher part. During the epidemic, cases occurred in both parts of the town, but were more numerous in the lower part. At least three to four hundred cases occurred in a population of about four thousand. In this estimate only typical cases, seen by Dr. Losa, are considered. Very few children were attacked, but otherwise age seemed to make no difference, youths, adults and old people suffering alike. During rainy periods, cases ceased to appear, but after two or three days' dry weather fresh cases used to be observed.

All cases, except one, had black vomit and melaena; they had also conjunctival injection from the onset and, by far the larger number, at a later stage, jaundice. There was intense headache and backache, '*coup de barre*.' High fever and oliguria were observed, but no thermometer was used, and urines not examined. Epigastric pain was a frequent, but not a constant symptom.

Dr. Losa's general impression was that the cases were of a comparatively benign type, though with well pronounced characters. The mortality was, however, high, being about one-third of the cases observed, but Losa believes this to be due principally to the extensive use of venesection which was practised by Indian quacks. Thus, he remembers the case of a lady, already in well-established convalescence, whom he left at 8 p.m., when she was conversing and feeling well; shortly afterwards an Indian performed an abundant venesection, whereupon she died in the course of a few hours.

Dr. Losa's treatment consisted in the administration of purgatives. Potassium permanganate was tried without any effect whatever.

Dr. Losa believes that the infection was carried to Tizimín from Valladolid (at a distance of about 50 kms.), where several cases had been observed in Mexican soldiers, then present at that place. From a ranch near Tizimín an Indian went to Valladolid; he was shortly afterwards taken ill at the ranch, and was brought to Tizimín in a late period of the disease, vomiting blood, and died soon after. In the house where he had died a lady was taken ill, and also died. Dr. Losa states, according to memory, that the interval, between the death of the Indian and the onset of the disease of the lady, was less than a fortnight.

Dr. J. Palomeque reports the following cases:—

1. *June*, 1878.—Epidemic in Mérida. J.B., 4 years, white, born in Mérida, and never been outside the city, was taken ill with a continuous fever which lasted approximately a week, with typical symptoms of yellow fever, except haemorrhages. Recovery.

2. *July*, 1878.—At a time when a severe outbreak reigned in Mérida. N.C., boy of 6 years, white, born in Mérida, and at that particular time staying in the neighbouring port of Progreso. He had never been outside Yucatán. He was taken ill with all symptoms of yellow fever, except black vomit and other haemorrhages. Treatment: Purgatives. Recovery.

3. *July*, 1878.—Severe outbreak in Mérida. N.R., girl of one year and a half, white, was taken ill at a ranch at a distance of about 4 kms. from Mérida, having been taken out into the country because of some dentition troubles. She presented all symptoms of yellow fever, including black vomit, anuria and cerebral phenomena. Death on fifth day of disease.

4. *August*, 1881.—Outbreak in Mérida. N.J., child of six years, white. All symptoms of yellow fever except black vomit and other haemorrhages. Recovery.

5. 1881.—At the time of epidemic. M.N., boy of 7 years, son of native parents. The boy was born in Espita, where he had lived until he came to Mérida, in the year 1881. He suffered from a severe attack of yellow fever, with haemorrhages as a predominant feature: haematemesis, epistaxis, bleeding from the ears, haematuria and cutaneous petechiae. Recovery.

This patient belonged to a group of individuals from the same town, who were living in the same house in Mérida. They were attacked by the disease in more or less severe forms, but eventually all recovered.

6. *February*, 1885.—Boy of 5 years, white, born in Izamal, son of native parents. Came to Mérida and stayed eight days. He was then taken ill, and taken back to Izamal; during the return trip, cerebral phenomena developed, and, in the course of the following three days, other symptoms of yellow fever. Death.

In the same house various other cases were observed in adult Creoles, but no other death occurred.

7. *February*, 1890.—At the time of epidemic. E.D., boy of 12 years, white, born in Mérida. Had never been outside Yucatán. All symptoms of yellow fever, including black vomit and anuria. Death.

8. *May*, 1895.—At a time when no epidemic of yellow fever was present. J.C., boy of 9 months, white. The child had been born in Mérida, and had never been outside the city. Black vomit, anuria, cerebral phenomena and other symptoms of yellow fever.

Dr. A. Molina remembers the following cases:—

1. 1879.—A.P., a native boy belonging to one of the prominent families in Mérida, arrived from Progreso with fever. He vomited black blood and died with universal jaundice.

2. 1883.—R.R., native child, seen by the late Dr. Doudé, who diagnosed yellow fever. Patient had black vomit. Recovery.

Dr. Molina remembers also that there was, in 1857 or 1858, an outbreak of yellow fever with epidemic character in Ixil. The late Dr. M. Arias was the physician in charge of these cases.

A short time afterwards there was a similar outbreak in Valladolid, which was also observed by Dr. Arias.

Very few foreigners, or none at all, were present during these outbreaks.

In 1876 there was an epidemic outbreak in the hacienda Calcehtok, situated near Maxcanú, on the main road from Mérida to Campeche. This outbreak started with a few cases; in the following weeks numerous cases occurred, and the whole outbreak lasted about a month.

Before the outbreak in Calcehtok had terminated, another developed in the neighbouring hacienda Chaktún, during which even more numerous cases occurred. This outbreak lasted one month and a half.

In both outbreaks the patients were native Indians. Dr. Molina does not remember whether atypical cases occurred before the beginning of the epidemics, but he does not consider it likely that the physician would have been called to see mild cases.

Both Dr. Molina and Dr. Palomeque, who are two of the most experienced practitioners in Mérida, are of opinion that yellow fever occurred more frequently in natives in earlier times than nowadays; they suggest the explanation that Indians in the old times lived more isolated and were, therefore, less exposed to an immunizing infection in childhood.

Dr. A. Canto:

1892.—C.B., two and a half years. This girl, who was born in Ticul and lived in Progreso, died of yellow fever in Progreso, in September, 1892. She had high fever and black vomit.

This is the only case of yellow fever in a native which Dr. Canto remembers to have seen during a practice of 21 years.

Dr. F. Casares:

1. *May*, 1893.—F.C.C., boy of 5 years. Patient was seen for the first time on the second day of disease; he had then a temperature of 39·5° C., the urine was scarce, the tongue coated, with red borders.

Rachialgia and epigastric pain were present. 3rd day: temperature 38° C. at 8 a.m., and 37·5° C. at 5 p.m., conjunctival jaundice, urine scarce, nausea, and bilious vomits. During the night the temperature went down to 37° C. 4th day: temperature at 8 a.m., 38·5° C. Jaundice increased, and vomits became more frequent. The diagnosis of yellow fever was confirmed by Dr. Palomeque. The disease ran its course and terminated in recovery.

2. *July*, 1904.—M.C., girl of 7 years, seen on 8th day of disease in a state of agony. She died two hours later. Black vomit and universal jaundice were observed, and the information obtained corresponded to a case of yellow fever.

3. A native boy of 13 years died of yellow fever on a ranch near Tzitás, at the time of an outbreak in the latter place. The boy, however, had not left the ranch.

Dr. E. Urzais:

March, 1906.—A boy born in Mérida of native parents went with his family to Guaymas, on the pacific coast of México, at the age of about two years, and returned when about five years. A short time after his return he was taken ill with yellow fever, and died after three days' disease. There was high fever, black vomit, jaundice and albuminuria, but not anuria. It is uncertain whether Guaymas should be considered a yellow fever place.

Dr. F. Colomé:

1. Boy of 3 years. The disease in this case lasted eight days, and the following symptoms are remembered to have been present: Temperatures between 39° and 40° C., conjunctival congestion, bilious and, later on, haemorrhagic vomits, in small quantity, but with characteristic aspect. Epistaxis, slight jaundice and slow pulse were also observed.

2. A boy of 5 years was taken ill with febrile temperatures about 38·5° C. and bilious and haemorrhagic vomits.

Dr. C. Dominguez:

November, 1900.—Native boy with continuous fever for four days, remission on the fifth day, and renewed rise of temperature for two days, after which time death ensued. There was anuria for over 24 hours, and 'chocolate coloured' vomit shortly before death. The body assumed an intensely yellow tint at the time of, or immediately after, death.

Dr. B. Enriquez:

1909.—Child of 2 years, born and living in Mérida. Fever, black haemorrhagic vomit, melaena and jaundice. Death.

Dr. J. Rivero:

Cases observed in Tizimín, *March*, 1912:

1. A native boy (Mestizo) was seen on fifth day of disease. He had a temperature of 40° C., a pulse of 120 and dyspnoea. There was abdominal distension and pain. Liver and spleen were found of normal size. Convulsions were present. Urine scarce. Black vomit, like that observed in yellow fever, set in, and afterwards coma and death.

2. A few days later Dr. Rivero was called to see a girl of two years, a native Indian. She had then, on the fifth day of disease, a temperature of 38·5° C., filiform pulse, dyspnoea and other symptoms as in the previous case, except convulsions and oliguria. She died on the sixth day after having vomited dark blood.

3. The third case was that of a native girl of three years, who was taken ill with symptoms of bronchitis, but, after four days, the same symptoms as described in the preceding cases made their appearance, and the patient died on the sixth day, in coma, having vomited black blood, like the vomits in yellow fever, during the last two days of the disease.

Dr. Rivero did not make the diagnosis of yellow fever, but has afterwards told me that he does not now doubt, that the cases were really of that nature, and that he would not hesitate to make the diagnosis in similar cases in future. The reason why he did not make the diagnosis at once was, that the cases occurred in natives.

Dr. A. Lara informs me that in the district 'Los Chenes,' in the neighbouring state of Campeche, there is frequently observed amongst the 'chicleros' (collectors of chewing-gum) a febrile disease with the symptoms of severe yellow fever, and often ending fatally. Blood, as a rule black, is frequently vomited, and jaundice is invariably present. It is commonly said amongst the overseers on the haciendas that a case may be considered hopeless if there is suppression of urine, whilst the outlook is considered comparatively favourable if the patient continues to pass urine in approximately normal quantity.

This disease is generally known as malaria, in the form of bilious remittent fever, and with vomiting of blood.*

The 'chicleros' are, with few exceptions, natives of Campeche, Yucatán, or some other place on the coast (Tabasco, Veracruz). Non-immune foreigners very seldom visit the country.

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* It was my intention to visit 'Los Chenes' with the object of observing some of these cases. No report, however, was received from this place during my stay until about a week before I left Yucatán. As it was uncertain whether I could return in time to take the steamer, I did not take that risk, but Dr. Lara went out alone and brought back blood specimens from two cases. These cases, however, were not typical yellow fever, and in both *Plasmodium praecox* (very scarce), but no *Paraplasma*, was found in the blood.

Dr. E. Erosa likewise informs me that in Cansahcab he has often seen cases diagnosed as malaria, which presented somewhat peculiar symptoms. After an initial chill there was a nearly continuous fever of three or four days' duration, with temperatures between 39 and 40° C. There were observed, moreover, bilious and afterwards haemorrhagic vomiting and malaena. No blood examinations have been made.

4

In the first week of January, 1912, I was invited by Drs. Canto and Vega to see several patients, native Indians, who had been received in their wards, and who presented somewhat peculiar symptoms. When I saw the patients—there were seven or eight of them—they were all convalescent, and the only symptoms which I could observe were universal, but not intense, jaundice and petechiae in the mucosa of the palate. Liver and spleen were not enlarged, the blood did not contain malarial parasites. No fever had been observed whilst patients had been in hospital. Of their history before entering hospital only very incomplete data could be obtained, as the patients spoke no Spanish, and, moreover, with the cautiousness common in Indians, gave as little information as possible. They had evidently suffered from an acute febrile disease, some for two, some for three, four or five days. They were all farm labourers from the hacienda 'Kambul,' near Motul; a number of similar cases had occurred at the hacienda, and several patients had died.

No more patients of a similar type were admitted to the hospital during the following weeks, and I heard nothing more of the matter until January 19, when Dr. Betancourt brought blood smears from a patient at Kambul, to Dr. Hernandez, for their examination. He told me that he had observed a series of cases of pernicious malaria at Kambul. Dr. Hernandez, however, found no malarial parasites, and gave me the slides for examination. After a prolonged search I found a few *Paraplasma* *flavigenum;* malaria parasites were entirely absent in two big smears. Before further information had been obtained, I went out on January 25 with Dr. Casares to see a suspicious case in Motul, and, whilst we were in that town, we were advised that a patient was in a very severe state at Kambul with symptoms of yellow fever, and that our presence was desired. When we arrived at Kambul patient had already died, and the hut where he had lived was being fumigated. We were told that the patient had been ill with high fever for five or six days, and had vomited blood during the last two days; a shirt was shown, soiled with dark blood. We had the corpse taken out of the hut: the spleen dulness was not enlarged, there was jaundice of the skin, and especially of the sclerae. I endeavoured to obtain material for microscopic examination by puncturing the spleen, but got no satisfactory result. I therefore proceeded to a post-mortem examination, which necessarily had to be very rapid and incomplete, standing, as we did, in the open air in an almost dark night. Spleen, liver and left kidney were examined. The spleen was of normal size, consistence and colour. The liver was of about normal size, very yellow, with small, scattered patches of a darker colour, and some hyperaemic patches; consistence very soft. The kidney was slightly enlarged, congested, with yellowish stripes and patches in its substance.

Subsequent examination of smears from spleen showed absence of *Plasmodium*, and presence of *P. flavigenum*. Microscopic examination of liver sections showed advanced fatty metamorphosis, and other characteristics of yellow fever, and in the kidney sections lesions were found which corresponded to the diagnosis of acute parenchymatous nephritis, made at the post-mortem.

At the hacienda we were also informed that a woman had been taken ill the same day; we found her with high fever, headache and backache, and it was arranged that she should be transported to the lazaret the next day.

After our arrival at Mérida next morning, Dr. Casares took the necessary measures to prevent further spread of the infection. Three patients, who had arrived at the hospital from Kambul one or two days before, were transferred to the lazaret, and a mosquito brigade was despatched to Kambul.

The history of the outbreak was now carefully gone into and discussed with Dr. Betancourt, who admitted that some fatal cases occurring in Kambul might have been yellow fever, but considered it probable that there had been, at the same time, an outbreak of malarial fever. The foreman of the mosquito brigade received orders to collect mosquito larvae; these I examined at the laboratory together with others which Dr. Betancourt had brought me. Most larvae were *Stegomyia*, and some *Culex*, but no *Anopheles* were found. On the night which we spent at Kambul I caught a few living mosquitos, all *Culex*.

For the following notes of cases which occurred at Kambul I am indebted to Dr. Betancourt.

1. *December* 11, 1911.—S.B. High fever until death. Black vomit and anuria one day before death, which took place on the tenth day.

2. *December* 14, 1911.—P.C., 25 years, 6 days' illness. Black vomit on sixth day. Daily chills. High temperatures all through the illness. Death.

3. *December* 17, 1911.—F.C., 10 years. Hyperaemia of sclerae. Chills and cramps. Urine very dark. Black vomit and diarrhoea on the eighth day. Abundant epistaxis. Anuria the last day. Death after 8 days.

4. *December* 18, 1911.—H.C., 35 years. Scleral jaundice. High temperatures. Black vomit and stools. Anuria. Death after 8 days' illness.

5. *December* 30, 1911.—P.B., 40 years. High temperatures until one day before death. Black vomit and stools. Anuria one day before death. Death after 8 days.

6. *January* 3, 1912.—J.T., 22 years. No elevation of temperature measured. Bilious vomiting and diarrhoea, chills, and cramps. Death after 5 days.

7. *January* 17, 1912.—M.C., 40 years. Temperature 38·3° C., P 100. Tongue coated. Epigastric pain. Bilious vomit. Subdelirium. The next morning symptoms had vanished, and patient was apyretic (temperature not taken). No more particulars until death took place, on January 25.

This is the same case which we saw after death, and of which particulars are given above. It would appear that there has been a remission of the symptoms on January 18, as patient seemed apyretic on the morning of that day, and as his relatives date his illness from only five days before death.

To these fatal cases we may add that of one of the patients who were transferred, on January 26, from Hospital O'Horán to the lazaret, and in which death occurred a few days later.

8. *January*, 1912.—S.C., 31 years. (Chart XI).

January 26.—Entered lazaret, from Hospital O'Horán, on 6th day of disease. Congestion of face and conjunctivae. Light scleral jaundice. Some restlessness. Intense headache and backache. Epigastric pain, increasing on pressure. Nausea. Tongue coated, with red borders. He is given a purgative, which is immediately vomited.

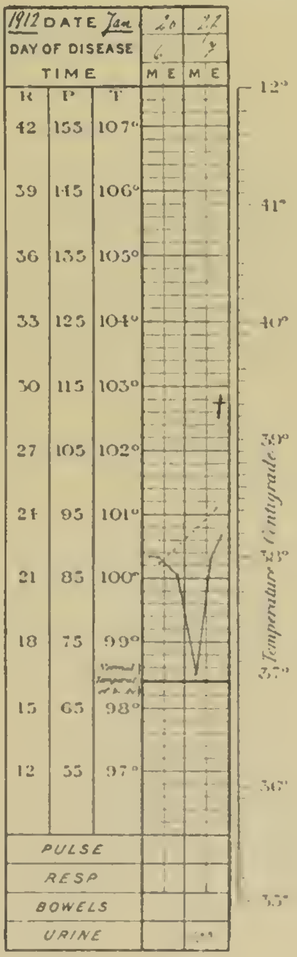


Chart XI.

During the night insomnia. Restlessness increases. Mucous and bilious vomiting.

January 27.—In the morning black vomit, which continues during the day. Patient is agitated and delirious. Pulse very weak. Death at 3 p.m.

Post-mortem examination, January 28.

Body well preserved (on ice). Rigor. Universal jaundice, particularly intense in the sclerae. Livid patches on back, shoulders and thorax.

Jaundice of adipose tissue, serous membranes, and intima aortae.

Hyperaemia of brain and meninges.

Hyperaemia and oedema of lungs. Oedematous liquid yellow. Nodules of congestion scattered in different parts of the lungs.

Pericardial liquid yellow, about 50 c.c. Small fibrinous patches on pericardium.

Liver 26 × 16 × 9 cms., 1300 gms., of a yellowish red colour, with some yellow, and other red, patches, and distended vessels. Capsule smooth and transparent. Interior more pale and yellow than surface. Consistence diminished. Fatty, sanguinolent liquid expressed from cut surface. Gall bladder filled with normal looking bile. Bile ducts patent.

Spleen 13 × 8·5 × 3·5 cms., 170 gms.; surface, consistence, and colour normal.

Pancreas, 17 × 4 × 3 cms., 120 gms., hyperaemic.

Right kidney, 12 × 7·5 × 4 cms., 150 gms. Surface shows slight congestion of stellate veins, on pale ground. Medullary substance hyperaemic, cortex pale yellow, with no haemorrhages. Consistence normal. Mucosa of renal pelvis intensely yellow, contains small ecchymoses. Left kidney, 11·5 × 6·5 × 4 cms., 150 gms., similar to the right.

Suprarenal capsules without alterations; in particular, no haemorrhages.

Stomach: All over the anterior wall haemorrhagic patches are seen in the mucosa; on the posterior wall there are less numerous ecchymoses, and a few small superficial ulcers. In the pyloric portion haemorrhages are more prominent.

The duodenum shows numerous haemorrhagic patches, especially corresponding to the mucosal foldings.

The jejunum presents also some ecchymoses, forming transverse stripes which correspond to the valvulae conniventes.

The ileum presents no ecchymoses, but hyperaemia.

Large intestine: hyperaemia.

Vermiform appendix: petechiae.

The urinary bladder contains a small quantity of icteric urine, and shows hyperaemia of mucosa.

Thus, the post-mortem findings in this case were typical of yellow fever. The prominent features were universal jaundice, haemorrhagic affection of stomach and upper part of intestine, fatty metamorphosis and hyperaemia of liver, acute nephritis, hyperaemia of lungs, intestines, and meninges.

Shortly afterwards, the following fatal case occurred at Kambul, but it seems very doubtful whether it has been of the same nature. In this case the blood was not examined.

Clinical history by Dr. Betancourt.

February, 1912.—C.C. Habitual alcoholist. Fell ill February 2, in the afternoon.

February 2.—Temperature at 4 p.m., 38° C., at 6.30 p.m., 40° C. Tongue coated. No jaundice. Urine scarce, dark. Pulse 104.

February 3.—Temperature 39° C. at 7 a.m., 39·8° at 6.45 p.m., 39·2° at 8 p.m. 50 c.c. of urine in 24 hours, very dark. Bilious vomiting. Fifteen ascaris vomited.

February 4.—Temperature 39°-39·3°. Pulse 110. Anuria.

February 5.—Temperature 38·5°-38·7°. Pulse 100. Respiration 48. Sclerae hyperaemic. Extreme anxiousness. Tongue red. Gums normal. Tympanism. Death at 11.30 p.m.

Dr. Betancourt observed also a number of non-fatal cases, occurring at the same time, at Kambul. As he visited the hacienda only once a week, from evening to next morning, his opportunity for making observations was necessarily very limited, and his notes are consequently very brief.

1. S.B., 11 years. Chills, headache, nausea, bilious diarrhoea. Tongue dry and coated, with red tip.
2. P.B., 3 years. Bilious vomiting and diarrhoea.
3. M.T., 50 years. Epigastric pain.
4. C.B., 7 years. Bilious vomiting and diarrhoea.
5. J.M., 25 years. Bilious vomiting and diarrhoea. Chills and acute cephalalgia.
6. I.C., 20 years. Temperature 39·5° C. Bilious vomiting and diarrhoea. Epigastric pain. Hiccough. Urine scarce, dark.
7. F.T., 25 years. Temperature 38° C. Intense headache. Chills. Profuse sweat.
8. J.C., 20 years. Temperature 39·3° C. Intense headache. Chills. Tongue coated. Bilious vomit.
9. L.C., 8 years. Temperature 39·5° C. Tongue coated. Bilious vomit and diarrhoea. Urine scarce, dark.
10. C.C., 14 years. Temperature 39° C. Intense headache. Chills. Bilious vomit.

11. C.C., 7 years. Temperature 39° C. Chills. Headache.

12. P.B., 25 years. Temperature 39° C. Headache, epigastric pain. Bilious vomits and diarrhoea. Urine scarce, dark.

13. E.B., 30 years. Temperature 39° C. Cephalalgia, epigastralgia. Bilious vomiting and diarrhoea. Light cutaneous and scleral jaundice.

14. G.C., 30 years. Epigastric pain.

15. C.T., 30 years. Temperature 40° C. Cephalalgia. Bilious vomiting and diarrhoea. Epigastralgia.

16. P.B. Temperature 40° C. Bilious vomits and diarrhoea.

It is, of course, impossible to make a definite diagnosis of these cases, but, in view of the fact that two of the fatal cases (Nos. 7 and 8) were, by post-mortem examination, proved to be yellow fever, and all the others, except case 6, can almost to a certainty be pronounced to have been of the same nature, it seems very likely that the non-fatal cases have also been yellow fever. It must be remembered that they all, fatal and non-fatal, occurred within less than two months, and that it appeared evident that they all belonged to one and the same disease. It has also to be considered that in no case was the diagnosis of malaria, which was the one prominently brought into discussion, proved by examination of the blood. No *Anopheles*, but *Stegomyia*, were found in the infected locality. We had, at the same time, numerous cases of malaria under observation, but none from that part of the country. It is remarkable that there were several children, even one of 3 years, amongst the non-fatal cases, whilst the youngest patient amongst the cases with a fatal issue was 10 years old.

The position taken by the Health Authorities was that the fatal cases were declared as yellow fever, but the non-fatal cases were not. A diagnosis of yellow fever was, however, made in two cases, which ended in recovery, and which were observed in the lazaret, namely, the two patients who were transferred from the hospital on the day of our return from Kambul. The following are the histories of these two cases:

January, 1912.—P.C., 32 years. (Chart XII). Patient stayed in hospital one day before he was transferred to the lazaret. Whilst in hospital he had febrile temperatures. After his arrival at the lazaret there was a single, slight rise of temperature, after which normal or subnormal temperatures were observed. The pulse rate also went down soon after, and became as low as 42. There was light jaundice.

The *blood* contained *P. flavigenum*, but no malarial parasites.

Urine: Sp. gr. 1·022. Reaction slightly alkaline. Indican reaction faintly positive. Urobilin present, but no bile pigment, and no haemoglobin. Diazo reaction negative. Albumin 0·25 °/₀₀. No casts, but some cylindroids, and renal epithelia. Leucocytes and erythrocytes absent.

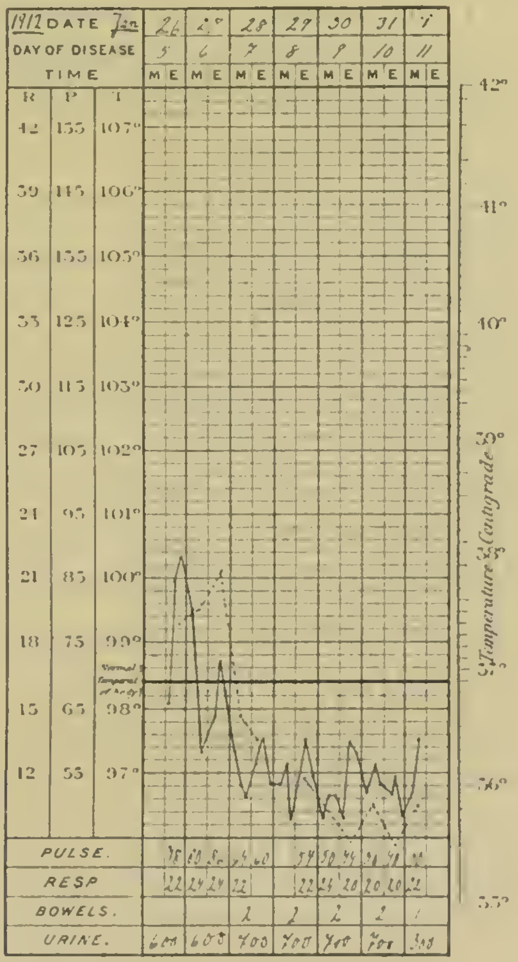


Chart XII.

January, 1912.—J.R., 30 years. This case was very similar to the foregoing, with the only differences that the highest temperature observed in the lazaret was 37·3° C., and that the urine contained only a trace of albumin.

In the first of these two cases *P. flavigenum* was found, but not in the second. Both patients had almost recovered at the time when the blood examination was made, but only the second was apyretic. *Plasmodium* was absent in both cases.

In the case of the woman, whom we sent from Kambul to the lazaret, yellow fever was not diagnosed clinically. The official diagnosis was gastric fever, but as febrile symptoms, headache, and temperature rises up to 39° C. were the prominent features, and the illness was of a few days' duration only, the diagnoses principally considered were, in fact, those of malaria and yellow fever. Malarial parasites were absent, on repeated examinations of the blood, but *P. flavigenum* was found; considering also the connection with the other, confirmed, cases, I feel confident that this was a case of yellow fever.

All patients from Kambul were pure Indians, belonging to the race of Mayas, the inhabitants of Yucatán at the time of the Spanish conquest; these Indians still form the principal part of the population in the country districts.

Two problems present themselves in connection with this and similar outbreaks, namely, why yellow fever is so seldom observed among the natives, and how, this being the case, it is to be explained that it does occur occasionally. There is, as already mentioned, little doubt that the reason is to be found, in the first case, in an immunity acquired through atypical attacks in childhood. The second problem is, perhaps, brought nearer to its solution, when we consider that in this particular outbreak, and in several others referred to, yellow fever broke out in small communities, living in somewhat isolated places, and having but little communication with larger centres. The infection may have died out, in the absence of sufficient material, and a non-immune generation may have grown up.

5

These reports may serve as illustrations, demonstrating the fact that yellow fever sometimes occurs, in its typical forms, in natives and continuous inhabitants of endemic areas. It should be emphasized that the cases observed in the city of Mérida occurred in children exclusively, whilst in the country districts cases were observed in adults also.

The occurrence of typical cases in natives is, however, always exceptional. This fact is, according to the now generally accepted opinion, due to the coincidence of two circumstances: that yellow fever in children as a rule is observed in atypical, and often benign, forms, and that practically all natives are attacked in childhood.

These two points have never been proved. The second one represents a conclusion arrived at from consideration of the epidemiological facts which, in view of our actual knowledge of immunity factors, do not seem to admit any other explanation, although the existence of a certain amount of hereditary immunity may enter into the theory as a factor of some importance. The first point is not so much the result of direct observation as a logical deduction from the second one.

It is quite true that we can, at present, see no other way of explaining the epidemiology of yellow fever, but it is true as well that our position as epidemiologists would be considerably strengthened, if the theory could be proved by direct observation. Clinically there seems to be no possibility of doing so, nor does it seem likely that any laboratory method short of the demonstration of the parasite could give sufficient evidence. I was, therefore, anxious to investigate the presence of *P. flavigenum* in the blood of native children; but I have, unfortunately, had very little opportunity of doing so. Investigation seemed more urgent still in cases, confirmed or suspected, of yellow fever, and, moreover, it did not prove easy to obtain blood from very young children. My material is, therefore, in this respect very small.

I had examined, on two or three occasions, the blood of children with febrile diseases, but with negative result in each case. At last I found a small number of parasites in some smears which were brought me by Dr. Hernandez, from a child with a febrile disease; yellow fever was not suspected. It was impossible to obtain more specimens from this case, as the child died on the following day.

Dr. D. Hernandez's case:

May, 1912. L.R.L., native girl, 13 months old. No previous illness. May 5, in the afternoon, it was observed that she was feverish; in the evening the temperature was 39°C. Next morning 40° C., and during the day 39·5° C. to 40° C. Vomiting, and one green, foetid evacuation. The following day, May 7, temperatures between 39° C. and 40° C. Urine very scarce. No enlargement of liver or spleen could be demonstrated. No sign of affection of respiratory system. The child died in the forenoon of May 8. The temperature continued high to the last, and there was no urine since the previous day, when a few cubic centimetres had been collected, which contained albumin and numerous hyaline and granular casts. There were no symptoms of meningitis. No jaundice.

The chief feature in this case was a severe febrile state with but slightly pronounced local symptoms. The symptoms from the digestive tract hardly explain in a satisfactory way the high temperatures and the fatal issue. The whole picture is that of a general infection, and albuminuria is thus easily explained. Whilst it would be impossible to diagnose the case as one of yellow fever from the clinical history alone, on the other hand the symptoms described are in no way opposed to this diagnosis.

I consider this case very important, and I believe that we are here on a line of research which deserves to be followed up.

With regard to the possible existence of microbe carriers, I must refer to the discussions on this question in sections I and VI.

IV. *PARAPLASMA FLAVIGENUM* IN CONFIRMED CASES

The blood was examined microscopically in sixteen cases, diagnosed clinically as yellow fever, and in one in which this diagnosis was made post mortem. In the latter case, that of M. C., of Kambul, the *Paraplasma* was, in fact, found in a blood-smear taken at the beginning of the disease, but I was not aware, until some time after, of the fact that this smear belonged to the same patient on whose body I performed a post-mortem examination at Kambul.

In the sixteen cases *P. flavigenum* was found in all but one. The negative case was that of J. R., of Kambul, which is mentioned in the foregoing section. This patient was apyretic, and practically convalescent, at the time when the blood-smears were taken. It is not surprising that parasites may be missed at this stage, either because they are absent, or extremely scarce. In one of the positive cases there was considerable doubt about the diagnosis, the patient having entered the lazaret in an almost agonic state. She died less than twenty-four hours after admission, and the official diagnosis of yellow fever was not made public until confirmed by post-mortem examination. The following notes from this case are of some interest.

January, 1912.—P.M. (G.), 33 years, female, Mexican (from the interior of the Republic, probably from yellow fever-free place). (Chart XIII).

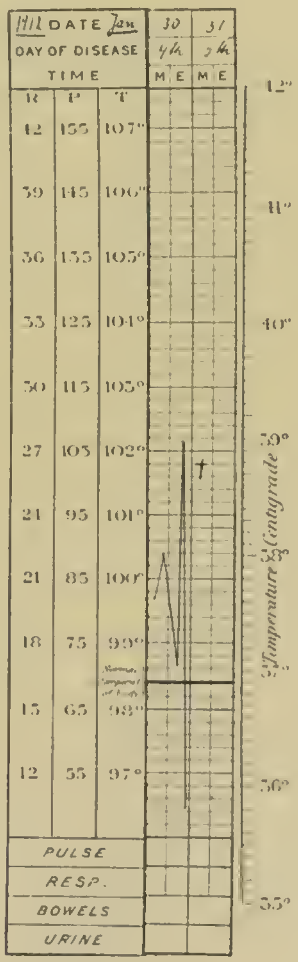


Chart XIII.

January 30.—Entered lazaret on 4th day of disease. Cephalalgia pain in limbs, epigastric pain, increasing on pressure. Conjunctiva hyperaemia. Scleral jaundice. Tongue coated, with red borders. Nausea, vomiting, foetid diarrhoea. Urine scanty, containing albumin. Subdelirium.

January 31.—Early this morning collapse, and death at 8.10 a.m.

Post-mortem examination about half an hour after death.

Stomach: The mucous membrane shows hyperaemia, petechiae, and ecchymoses; on posterior wall minute, superficial ulcers.

Duodenum, jejunum, and ileum: hyperaemia and, in the last mentioned, ecchymoses.

Colon: hyperaemia.

Vermiform appendix: hyperaemia and ecchymoses.

Spleen: 14 × 5 × 4 cms., 100 gms.

Liver: 27 × 17 × 6 cms., 1340 gms. Surface and substance yellow, with ecchymotic patches. Consistence considerably diminished.

Kidneys: Parenchyma yellow, with distended vessels. Very soft consistence.

Post-mortem diagnoses: Icterus universalis. Metamorphosis adiposa hepatis maximo gradu. Gastritis acuta ecchymotica maximo gradu cum erosionibus. Enteritis acuta. Ileitis acuta ecchymotica. Colitis acuta. Epityphlitis ecchymotica. Nephritis acuta duplex, cum metamorphosi adiposa. Cicatrices renis dextri. Hyperaemia meningum, et pulmonum. Struma. Cholelithiasis. Nodulus caseosus lienis. Urethritis ulcerosa. Cystes uteri. Cystes ovariorum. Helminthiasis (*Tricocephalus trichiurus* appendicis vermicularis).

For statistical purposes it is evidently correct to include not only this, but also the case of M. C., referred to above, in the list of confirmed cases, especially as in both the parasites were found whilst patients were alive. Thus we have 17 cases diagnosed officially as yellow fever,* in 16 of which *P. flavigenum* was found in the peripheral blood. Adding these cases to those of my last two series (1911, 1 and 5) we get 53 positive results in 57 cases. Including also my first series, in which the cases were not tabulated, the result is, approximately, one hundred and six positive cases out of a total of one hundred and twenty.

The following table indicates, in the present series, the days on which blood examinations have been made, and those on which positive results have been obtained. We have here to do with officially confirmed cases, and that means nearly always severe cases; the table should,

* In one of the Kambul cases (J. T.) the blood was not examined.

therefore, be compared with the one in the following section. The value of the table is considerably impaired by the fact that most cases have come under observation at an advanced stage of the disease. For diagnostic purposes, which are, in this connection, of paramount importance, results obtained during the first few days would have been of far more interest.

In the table only those of the confirmed cases are included, in which somewhat reliable data as to the duration of the illness were obtained.

CASE			DAY OF DISEASE																
No.	Name	Result	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1	T.A.	Recovery	...	...	...	÷	+	...	...	+	+ +	...	...	+	...	...	...	...	...
2	F.O.	Death	...	...	...	...	+ +	+ +	...	...	...	...	...	...	...	...	...	...	...
3	M.G.	Recovery	...	...	...	...	...	+	...	...	...	...	...	...	...	...	...	...	...
4	F.S.	Recovery	...	...	...	...	+	÷	+	÷	+	...	...	...	...	...	...	...	...
6	S.C.	Death	...	...	...	...	+	...	+	...	...	...	...	...	...	...	...	...	...
9	P.U.	Recovery	...	...	...	+	...	...	...	...	...	...	...	...	...	...	...	...	...
10	P.M.	Death	...	...	...	÷ +	...	...	...	...	...	...	...	...	...	...	...	...	...
11	O.R.	Recovery	...	...	...	÷	÷	...	+	÷	+	...	...	÷	...	...	...	...	÷
12	L.P.	Recovery	...	+	...	+	÷	÷	...	...	...	...	...	...	...	...	...	...	...
13	P.T.	Death	...	...	...	...	...	+	...	...	...	+	...	÷	...	...	...	...	...
14	A.D.	Recovery	...	...	...	...	...	+ +	+ +	÷	÷	...	+	+	+	+	÷	...	...
15	L.M.	Recovery	+	...	÷	...	...	...	...	...	...	...	...	...	...	...	...	...	...
16	J.L.	Death	...	...	...	+	+ +	+	...	...	...	...	...	...	...	...	...	...	...
17	M.C.	Death	+	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...

+ Presence of *Paraplasma*.

÷ Absence of *Paraplasma*.

Two signs indicate that the blood has been examined twice on the same day.

Blank space indicates that no blood examination has been made.

A more detailed study of the confirmed cases was impossible, because most cases came under observation at a late stage, and because those not in the lazaret could not be seen daily, and also because much time was given to the examination of the blood in control cases, which part of the expedition's work was considered particularly important.

V. *P. FLAVIGENUM* IN SUSPICIOUS CASES

A large number of patients were admitted into the lazaret as suspicious of yellow fever, i.e., non-immune foreigners with febrile disease. Most of them had malaria, others typhoid fever, tuberculosis, measles, angina, or other diseases, and a certain number had fevers of from two to five or six days' duration, with one or several of the following symptoms: headache, backache, congestion of face, jaundice, coated tongue, epigastric pain, nausea, vomiting, and albuminuria, for which no definite organic lesion could be held responsible. In most of these cases a symptomatic diagnosis—as gastric fever, bilious fever, or some similar affection—was made, in which no indication as to the etiology was expressed. In all cases admitted to the lazaret I examined the blood, often without having seen the patient, and in 30 cases I found *Paraplasma*, 13 of which were later confirmed as yellow fever. On the other hand, *Paraplasma* was found in 7 cases seen in the city or country, in 3 of which yellow fever was officially diagnosed. Thus, *Paraplasma* was found in 21 cases in which yellow fever was not diagnosed, but which were all febrile cases of short duration with no definite local symptoms. The clinical histories of several of these cases are given in section 2, and the following is a list of the various diagnoses under which they were returned: Gastric fever, 'embarazo gástrico,' malaria (no parasites found), bilious fever, acute gastro-enteritis (in an infant), acute bronchitis, dysentery, no diagnosis. It may require a few words of explanation how such diagnoses as bronchitis and dysentery should have been returned, as each of them was in one case. The first was that of a newcomer who was admitted to the lazaret on the third day of disease with fever (38·5° C.), hyperaemia of conjunctivae, coated tongue, and bronchitis. Bronchial affections are occasionally seen in severe cases of yellow fever, but in this case I should be inclined to believe that there has been a coincidence of two infections. In the other case the diagnosis of dysentery was suggested by the excessive effect of strong purgatives, as shown by the subsequent course. This patient was seen on the fifth day of his illness with a temperature of about 39° C., and all symptoms disappeared in less than two days, which would evidently not have happened in a severe case of dysentery. The diagnosis given in most cases was gastric fever, a common name for mild cases of yellow fever.

The following table shows the days on which *P. flavigenum* was found in the blood, in those cases in which reliable data were obtained: —

Case			Day of Disease													
No.	Name	Result	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1	F.P.	Recovery	+	+ ÷	÷	...	...	...	...	...	...	...	...	...	...	...
2	C.R.	Recovery	...	...	...	...	+	...	÷	...	...	...	...	...	...	...
3	R.B.	Recovery	...	+	...	...	...	...	...	...	...	...	...	...	...	...
7	M.H.	Recovery	...	...	+	...	...	...	...	...	...	...	...	...	...	...
8	E.C.	Recovery	...	+	...	...	÷	...	...	...	...	...	...	...	...	...
9	C.G.	Recovery	...	+	...	...	...	...	...	...	...	...	...	...	...	...
13	M.R.	Recovery	...	...	...	+	...	÷	...	...	...	...	...	...	...	...
16	H.S.	Recovery	+ +	+	+	...	...	+	...	...	...	+	...	...	...	÷
18	A.E.	Recovery	...	+	...	...	...	...	...	...	...	...	...	...	...	...
19	J.S.	Recovery	...	...	...	+	...	...	...	...	...	...	...	...	...	...
21	L.R.	Death	...	...	+	...	...	...	...	...	...	...	...	...	...	...

It results from this table that the parasites were observed, as a rule, at an earlier stage than in the confirmed cases which were generally more severe. This may be quite accidental, simply because these cases happened to enter the lazaret at a comparatively early stage of the disease. But it may also have occurred that parasites have not been found in mild cases admitted at a later stage, because they had already disappeared from the blood. This explanation has a certain probability, since it is seen in the table, that the parasites have disappeared quickly in most cases in which repeated examinations have been made. An exception from this rule forms my own case, in which *P. flavigenum* was found even in the convalescent stage. In this case several of the blood examinations were made by Dr. Hernandez, but afterwards repeated by myself. I had also examined my blood several times before my illness, and, after returning to the laboratory, examined it again repeatedly, always with negative results.

VI. THE RÔLE AND NATURE OF *P. FLAVIGENUM*

In my earlier work I had, quite naturally, examined with special care the blood from yellow fever cases, the control material consisting in the numerous blood examinations occurring in the daily work in my laboratory. This time I proposed to lay special stress on obtaining a large control material. This I did by examining the blood from all cases admitted to the lazaret, from a number of patients seen in the hospital or with physicians in their practice, or from patients whom I had not seen, and, finally, from numerous healthy individuals. In each case I used the same microscope which I used in the yellow fever examinations, always working with the same 3 mm. apochromatic immersion objective (Zeiss), and No. 12 compensating eyepiece; at least one hour was dedicated to the examination of a smear, before it was declared negative. This was carried out in the malarial cases, as well as in those in which no parasites at all were found. The presence of malarial parasites caused but little difficulty. Very young forms, even of *Plasmodium praecox*, were easily recognized by their larger chromatin granule, but occasionally some slight doubt arose when remains of malarial parasites were seen in the erythrocytes, as a rule after quinine treatment. Such doubt, however, was soon solved by comparison with films containing *Paraplasma*. On specially important occasions, special precautions were taken; in such cases blood films were prepared, at the same time, from other individuals and treated all through in the same way as those which were of particular interest.

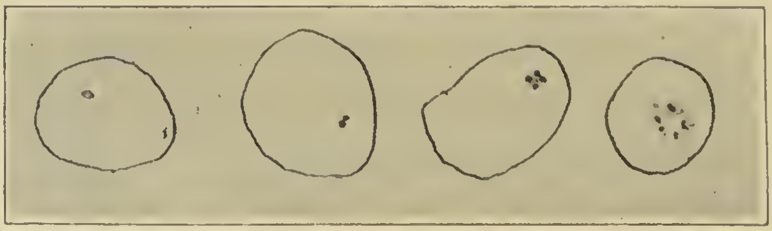
In this manner blood specimens were examined on 421 occasions, in each case at least one, and often two or three, slide-smears being thoroughly searched. In 136 cases malarial parasites were found, and in 283 no parasites at all; finally, in two cases, in which there was no suspicion of yellow fever, *P. flavigenum* was present in small numbers.

The two individuals, in which *P. flavigenum* was found, were young children seen in a school in Temax on the occasion of a visit which I made with Dr. Casares in order to study the sanitary conditions of that place, from which two yellow fever patients had been brought to the lazaret in Mérida. It was my intention to examine the blood of children with febrile disorders, but we had the opportunity of seeing only two such cases (enteritis), and in both the blood proved negative. We then examined the children in the schools, more with the object of discovering cases of malaria, than in the hope of finding cases of larval yellow fever. Blood-smears were taken from a number of children with a very slight increase of the spleen dulness (in no case was the spleen considerably increased). Amongst these cases were the two under discussion. As the microscopical examination was made after our return to Mérida, the children could not be identified; thus I cannot assert that they were in good health, but, at any rate, they cannot have been severely ill, since they went to school. They have certainly not been perfectly healthy, since they were selected for examination as suspicious of malaria. These two cases must be considered together with the two somewhat similar cases which I reported in an earlier paper

(1911, 1); in those, *P. flavigenum* was likewise observed in two individuals not suffering from yellow fever. The one was a young girl with anaemia, the other a boy with nephritis; both were natives.

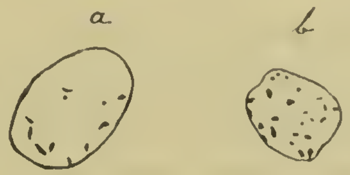
In these four cases we may possibly have to do with microbe carriers, in the true sense of the word—individuals harbouring parasites in their blood for a considerable length of time. But there is no proof that it is so. It may just as well have happened that the blood of these individuals has been examined during one of the repeated attacks of yellow fever, or, rather, infections with yellow fever parasites, which are supposed by various authors to occur with a certain frequency in natives, producing no characteristic symptoms, or that the individuals have been suffering from chronic infections.

With regard to its morphological characters I have nothing of essential importance to add to the descriptions which I have given in my earlier papers (1909, 1911, 1 and 5). The forms usually observed were the same small intracorpuscular bodies as formerly described. Free bodies were also found, both in the peripheral blood and in smears and sections of organs. The largest intracorpuscular forms were found in smears from liver (Plate I, fig. 20). No definite life cycle has been determined, but elements have been observed which it can hardly be a mistake to consider as division forms. When elements from various specimens are considered together, the following evolution apparently results (text fig. II).



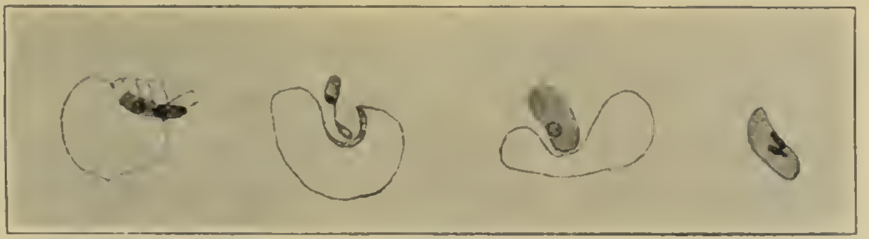
TEXT FIG. II.

Whether the last form represents the final stage of division, is very uncertain. The following two corpuscles, with inclusions, one (*a*) from a kidney section, and the other (*b*) from the peripheral blood, would suggest the possibility that there may finally result a much larger number of excessively small spores (merozoites) (text fig. III).



Text Fig. III.

As previously mentioned, several of the free forms are very similar, morphologically, to those which we know as gametocytes in other protozoa. Their extreme scarcity, however, makes it very unlikely that these should be the only elements on which the transmission by mosquitos has to depend. It is, of course, possible that intracorpuscular elements may develop further in the stomach of the mosquito. The following would appear to be the evolution of the large free forms (text fig. IV).



Text Fig. IV.

In earlier papers I have mentioned the presence of bodies enclosed in endothelial cells, as observed in sections of various organs. I have now to add that I have observed also apparently phagocytosed elements in both mononuclear and polymorphonuclear leucocytes, in the peripheral blood (Plate I, figs. 33-37). Large, chromatin-stained granules are frequently seen in the protoplasm of monocytes, in yellow fever, as well as in malaria, and especially in

Babesia-infections. The nature of these granules is not quite clear; in some cases there is little doubt that they represent phagocytosed parasites, in other cases they may belong to the cell, but it is remarkable that the nuclei are, nearly always, well preserved. They show some resemblance to the granules observed by Leishman (1912) in blackwater fever.

In Plate I typical forms from my expedition material are represented. The figures have been drawn from many different specimens, from different cases, and are obviously identical with those previously published. No definite statement can be made regarding their evolutional stage, but such data as are available will be found in the explanations of the figures.

On Plate II I have shown, in the first four rows, types observed on subsequent occasions in a single case in which blood specimens were obtained from the first day. As this was my own case, it happened, unfortunately, that I had no smears taken on the fourth and fifth days. On the third day only a few chromatin granules were observed, but no well-defined parasites. Thus, the four rows represent parasites from the first day, forenoon, first day, evening, second day and sixth day. On the first and second days they were very numerous, on the sixth scarce, on the tenth extremely scarce, and on the fourteenth they had disappeared altogether. On repeated occasions during the following weeks my blood was examined, and parasites were always absent, as they had also been before my illness.

The only other case, in which numerous blood examinations were made, was that of A. D. This patient came under observation rather late, but, in spite of this, there was a certain resemblance in the morphological characters of the parasites to those observed in my own case. On the first two days, i.e., sixth and seventh days of disease, numerous and very minute elements were observed, later on scarce, and somewhat larger, forms. The clinical history of A. D., as told by himself (see section on treatment), conveyed the impression that he was suffering from a recrudescence of his disease, when admitted to the lazaret. He had been ill for five or six days before with black vomit, apparently abundant, on the second day, and melaena on the third. On the fifth day he seemed better, but on the sixth he was in very bad condition, wherefore the people with whom he stayed, and who had hitherto kept secret that they had a case of yellow fever in their house, became afraid that he should die, and called a physician, who immediately sent him to the lazaret. After his arrival there haemorrhages set in afresh, as it seemed, after an interval of at least one day. This may be the explanation why in this case a similar series of parasites were found on the sixth and seventh day, as in my own case on the first and second.

I can say nothing new with regard to the zoological position of *P. flavigenum*, but must refer to the discussion in my last paper. Such forms as that represented in Plate I, fig. 20, certainly suggest a close resemblance to the genus *Babesia*, and many of the minute forms seem almost identical with the initial bodies seen in bovine or canine babesiasis; most larger forms, on the other hand, are distinctly different from *Babesia*. I must therefore uphold my formerly expressed view, that our parasite probably represents a new genus in the family *Babesiidae*.

No observations have, so far, been published on the subject of this parasite, except my own. Unfortunately, very little research work appears to be done at the present time on yellow fever problems, although many are still awaiting their solution, before the pathology of yellow fever can become fully understood. It seems also to have become a somewhat common belief that the yellow fever parasite could not be discovered by means of actually existing methods of investigation. I have previously (1911, 5) mentioned that this belief is without foundation in facts, and that not all investigators of yellow fever have taken this view; it may be added that Doerr (1911) in a recent paper has emphasized that the word filterable ought to be substituted for invisible (or ultravisible), as many authors have already done.

In my earlier papers I have already discussed some objections which had been made, mostly in private discussions, against my findings. Since then, a few criticisms have appeared, though none of them has been based upon actual observations on yellow fever. The most important is that of Schilling-Torgau (1912, 1 and 2), who has found, in human blood and in blood from various laboratory animals, intracorpuscular bodies very similar to those described by me; the elements which he has observed are, in his opinion, remainders of more or less hypothetical structures, which he regards as normal constituents of erythrocytes. This is, of course, a serious objection, being based, as it is, upon careful investigations. The only way to meet it was by a comparative study of blood from other individuals, in the same place, and with the same technique. This is what I have done now, and I think a better material for control, than the one discussed above, could hardly be obtained. This also answers the objection made at a discussion in Habana, by Dr. Guiteras, that I might have encountered an innocent parasite living in the blood of inhabitants of Yucatán.

The criticism of Agramonte (1912) I have dealt with elsewhere, but very briefly, as I was, at that time, at work in Mérida, with little time and very scanty literature at my disposal; I must therefore reluctantly return to it here. Agramonte infers that my staining technique is very poor; this opinion is not shared by his colleagues in Habana, nor do I think by anybody else who has a personal knowledge of my work. He says, further, that the parasite is very scarce, and that we know that yellow fever blood must contain a great number of parasites. This is precisely what we do not know. Supposing, for instance, that an ordinary smear contained two or three parasites, then 0·1 c.c. of blood would probably contain several hundred and 1 c.c thousands of parasites; we have no idea how many are required to produce infection. Moreover, his assertion is not correct, as considerably more than three or four parasites had been observed in one smear, already in my earlier series, though this was not the rule. It has not been the rule either, in the last series, but, exceptionally, much larger numbers have been found; for instance, in smears from the cases of A.D. and H.S. I have repeatedly counted over forty parasites in a very thin film. Agramonte says also, that the parasites have not been observed by me 'except from the fourth to the eighth day,' that we have 'no reason to believe that the parasite of any infectious disease may be demonstrated in the blood at any period when this blood is not infective,' and that 'experiments have demonstrated that yellow fever blood is not infective after the third or fourth day.' None of these statements is correct. I have mentioned already, in my first two publications on this subject (1909 and 1911, 1), the presence of parasites in the blood, on the third day; in this report I have mentioned their presence on the first and second day. With regard to the second point, it all depends on what is understood by the term 'infective.' We know that malarial blood, which contains schizonts, but no gametocytes, is non-infectious in mosquito experiments; and it is quite safe to conclude that any blood, which contains intracorpuscular parasites only, must be non-infectious in experiments with filtered serum. Thirdly, that yellow fever blood should be non-infectious after the third day of disease, is an assumption which has never been proved; this I have pointed out on several occasions, and shall not repeat the argument here; that it is so must be evident to everybody who studies the original literature. When Agramonte next says, that 'it is not possible to find two bodies alike in the same preparation,' it is entirely his own statement. I have often seen, and demonstrated, even in earlier cases, several bodies, very similar to each other, in one and the same film; in my last series, parasites with almost identical characters have been even numerous in certain smears. Agramonte's last objections, that the parasites show no analogies with other blood parasites, and, that they ought to be better observable in fresh than in stained specimens, are of very slight importance. I have not admitted, as Agramonte says, that there is no such analogy; on the contrary, I have repeatedly stated my opinion that the parasites appear to be similar to, though not identical with, various members of the family *Babesiidae*. With regard to the question of fresh, versus stained, specimens, I am under the impression that most workers consider the observation of fresh blood specimens even more difficult, and more exposed to misinterpretations, than that of stained. Agramonte's principal argument seems to be, that earlier investigators have failed to discover the organism which I have observed. This argument, of course, is utterly devoid of value; if it held good, no discoveries could ever be made. Only observations subsequent to my own, and in which a similar technique has been employed, can be considered in a critical discussion on this subject.

Before leaving this matter, I may, perhaps, be allowed one more remark, in self-defence. Agramonte says that I have misquoted several authors, and mentions particularly a paper by Carroll (1903). I must, therefore, again emphasize that what I have said is entirely correct. As already pointed out, on p. 128, Carroll's table of negative experiments contains seven cases in which the conditions are apparently fulfilled. In each of two cases two inoculations were made, under favourable conditions; thus, nine inoculations have given negative results (we might even say ten, if we included Case 22, in which the individual was not, as the others were, afterwards proved susceptible). Together with the 14 positive cases in Carroll's Table 3, we have thus to consider 14 positive results in 23 inoculations, precisely what I said in my paper referred to (1911, 5, p. 231). What Agramonte understands by 'conditions plainly adverse to infection' is entirely unintelligible.

Agramonte ought to remember that a charge of misquotation is a serious matter, especially as he tries to convey the impression that it has been made intentionally. He ought to state also what other authors he believes me to have misquoted, instead of speaking of several, and he would certainly learn that he is mistaken.

Cartaya (1912) has described intracorpuscular bodies observed in a case of glanders, discussing their possible identity with my *P. flavigenum*, but without drawing any definite conclusion, and Guiteras states, in a footnote to Cartaya's paper, that he has seen similar bodies in two cases of Icterus gravis. I have, through Dr. Guiteras's kindness, had the opportunity of examining specimens from these cases, and have seen the bodies referred to, but I have no doubt that they are different from those in yellow fever. Those in the case of glanders I regard, with Cartaya, as nuclear remains, and in the smears from Icterus gravis I found only one definite structure, which I believe to be a degenerated malarial parasite. The lack of figures illustrating the findings of Guiteras and Cartaya make a detailed discussion impossible.

Thus, I fail to see that the published criticisms should have thrown much doubt on the results of my observations. The essential question is, whether the bodies described are parasites or not. Once their parasitic nature accepted, their specific importance will have to be admitted also. A parasite which is found with such a remarkable constancy in a certain disease, can hardly fail to be its pathogenic germ. The weightiest objection, that the bodies might represent erythrocyte-elements, can only be answered by a reasoned study of the cases, in which the bodies have been found, and of control cases. This I have endeavoured to do in the foregoing pages, and, before leaving this subject, I would point out the remarkable fact, that whilst pathological alterations of the erythrocytes would be expected to occur with the greatest frequency in severe cases, and in advanced stages, this has not been so in my observations. In this connection my own case is especially demonstrative: parasites were most numerous on the first and second day, and the whole disease was so mild that one would hardly expect severe alterations of the blood to take place. My general state of health was good at that time, and no morphological alterations were found in the blood either before or after my illness. Supposing we had to do with alterations of erythrocytes, then we would have, in this and other mild cases, pathological alterations, which did not occur in much severer cases of other diseases. These alterations would, thus, be specific; but specific elements, similar to parasites, and occurring under conditions and with characters, as might be expected, are, logically, most likely to be parasites.

VII. DARK GROUND OBSERVATIONS

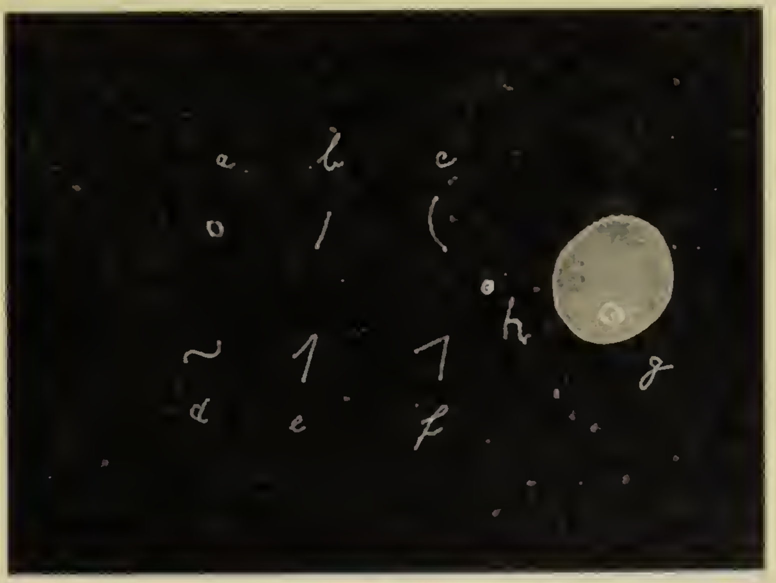
In my earlier work I tried in vain to obtain reliable results by the examination of fresh specimens of yellow fever blood. In a few cases I observed intracorpuscular elements similar to those seen in stained films, but I never felt quite sure of these observations. This time I hoped to obtain better results by the use of Zeiss's paraboloid condenser, and was not entirely mistaken, though I may say at once that this method has not, so far, brought my investigations any definite step forward.

I was, of course, very much interested in the examination of filtered serum, as I hoped to find minute elements which must be supposed to exist in the blood, being able to pass through porcelain filters, as filtered serum has been proved infectious. But the observations, which I made in a few cases, were negative, as I saw absolutely no elements which might be suspected of being living organisms.

In fresh blood, or unfiltered serum, on the other hand, there was such a multitude of small, motile bodies that it was quite impossible to make sure of their nature. On the whole, my impression was that free motile elements were somewhat more numerous in the blood from yellow fever patients than in other cases. Most of these elements were spherical, with no definite structure, and could not be differentiated from those observed in normal blood. There was considerable resemblance between these bodies and the granules of polymorphonuclear, neutrophile leucocytes. The number of such elements varied very considerably in normal blood. In my own blood they were generally rather scarce, but in that of several of my colleagues at the laboratory very numerous. They were more numerous shortly after a meal than several hours later. Thus, it seems strange that they should be found in considerable numbers in yellow fever cases, since all food was withheld from these patients, and I cannot suggest any explanation why it was so. The movements of these granules were very irregular, but appeared to differ from ordinary Brownian movements.

Other free, ovoid bodies, with a central granule, were evidently small platelets.

Besides the granules, I observed in several cases of yellow fever, and later also in blood from healthy individuals, some peculiar filaments. They were not present immediately after the preparation of a fresh specimen, but were first seen from half an hour to two hours later. They appeared at first as small, extracorpuscular rods, which in some cases seemed to take their origin from small, free rings; they developed subsequently into fine filaments, the length of which varied from one-fourth to almost the entire diameter of an erythrocyte. They had, generally, a distinct dot in one or, more frequently, in both extremities, and were very motile, possessing undulating, distinctly progressive movements. After several hours they became very numerous (text fig. V, *a*, *b*, *c*, *d*). Occasionally two such filaments

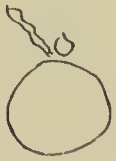


Text Fig. V.

were united, either in an end to end, or in different angular, positions (fig V, *e*, *f*).

These filaments bore a great resemblance to malarial microgametes, which I observed at the same time with dark ground illumination. The movements, in particular, were very similar. I felt, therefore, to begin with, when I had observed filaments in yellow fever blood only, very much inclined to the belief that they might represent some stage in the evolution of the parasite. But soon afterwards I found identical filaments in the blood of a few healthy individuals, notably, on repeated occasions, in that of Dr. Hernandez, though always less numerous than in yellow fever blood. In my own blood filaments were seen on the first day of my illness only, but not before that time nor after my return to the laboratory; during my illness no ultramicroscopical examination of my blood was made.

These filaments were observed in five cases of yellow fever and in, at least, two healthy individuals (in a third case a beginning formation of filaments seemed to take place, but none were seen fully developed). After my return to Liverpool I have examined blood of myself and of several other healthy individuals, with negative result in each case; this, however, might perhaps be due to the comparatively low surrounding temperature.



Text Fig. VI.

The nature of these filaments remains entirely obscure. They have certainly nothing to do with the red blood corpuscles, and are thus different from the bodies described by Nuttall and Graham-Smith (1906), and Balfour (1911). The only relation to blood elements which I can admit as possible, is that they might take their origin from platelets; the ring-shaped bodies, from which they were seen to develop, were not wholly unlike these elements. This origin, however, would not account for their peculiar shape and characteristic movements, features which surely suggest living organisms.

I was unable to find these filaments in fresh specimens with the ordinary condenser, but observed, in my own case, very similar elements in stained specimens (text fig. VI).

In the case of A.D., I observed, moreover, with the paraboloid condenser, small, motile, intracorpuscular bodies containing one or two extremely minute, intensely reflecting (probably chromatin) dots. They were very scarce, and were observed at a time when stained films showed numerous parasites.

This observation was confirmed by Drs. Hernandez and Palomeque, and several other medical men. One of these bodies is shown in text fig. V, *g*. A few very similar extracorpuscular bodies could be recognized, with some difficulty, amongst the multitude of free granules (text fig. V, *h*).

I have no doubt that these bodies were identical with those observed in stained specimens.

Thus, dark ground observation has, so far, not proved of great use in yellow fever work,* but it is quite possible that further investigations may give better results.

VIII. EXPERIMENTAL WORK ON GUINEA-PIGS

Marchoux & Simond (1906)** and Thomas (1907) have made experiments with the object of transmitting yellow fever to laboratory animals, especially chimpanzees, and have obtained some febrile reactions, but the results have not been very demonstrative.

This was not encouraging, but I reasoned that it might, perhaps, be possible to transmit the parasite, even should the injected animal not develop any pronounced pathological symptoms. I therefore resolved to make some experiments on guinea-pigs, the easiest animal obtainable which could be transported from a yellow fever free place to Mérida.

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* Otto and Neumann (1905) also failed to obtain results by this method.

** See also Marchoux's Review, in *Bull. Inst. Past.*, Par., 1907, V, p. 222, of Thomas's paper.

It was not considered advisable to experiment with any animals born in the country. Accordingly, three dozen guinea-pigs were sent by direct steamer (Leyland Line) from Liverpool to Progreso, and I received, three weeks later, thirty-five in Mérida; owing to the good care which had been taken of the animals on board the steamer, only three guinea-pigs died during the voyage, and, as two were born, the loss was almost made up for.

After their arrival, the guinea-pigs were kept in mosquito-proof cages, in order to avoid the possibility of casual infection. Blood specimens were examined from all animals experimented upon, before inoculation, and from several others, for the sake of control. In no case were parasites found in the blood, in non-inoculated animals.

The following technique was used in the experiments:—5 c.c. of blood were drawn from a patient by venepuncture, defibrinated, and injected into the heart of healthy guinea-pigs through the thoracic wall, after shaving and painting with tincture of iodine. The injections sometimes proved difficult, especially because the animals several times collapsed after the injection of a certain amount, about 0·5 c.c., of blood; when the injection was stopped, the guinea-pig quickly revived, and the injection could always be carried out successfully. In the case of injection from one guinea-pig to another, blood was extracted from the heart of one animal, defibrinated, and injected into the heart of another.

The following experiments were made:—

EXPERIMENT I, *February* 22, 1912. 1 c.c. of defibrinated blood from a yellow fever patient (P. T.) on the fifth day of disease was injected into each of two healthy guinea-pigs. In both cases there were slight oscillations of the body temperatures during the first seven days following the injections, whilst distinctly higher temperatures were recorded from March 3, onwards. As this apparent rise, however, took place just after I had discovered that sufficient care had not been taken in measuring the temperature, it cannot be considered of much importance. I found also considerable variations of the temperature in healthy guinea-pigs. The two inoculated animals remained, apparently, in good health, the one for more than a month, and the other for just over two weeks, when it was taken ill and died after a few days. Its fatal illness probably had no relation to the injection of yellow fever blood, since it occurred after an interval of two weeks, during which there had been no symptoms resembling yellow fever, and since several other guinea-pigs died at the same time with similar symptoms.

From each of these two guinea-pigs another was injected, and presented no definite rise of temperature, nor any other symptom.

EXPERIMENT II. On *March* 18, 1912, two guinea-pigs were injected with blood from a yellow fever patient (A. D.) on the seventh day of his illness. The results were negative.

The number of experiments made is very small, due to the circumstance that very few cases of yellow fever occurred after the arrival of the guinea-pigs.

The examination of the blood proved negative in all the guinea-pigs before inoculation, and in those of Experiment II, as well as in those of the second series of Experiment I. The two animals injected with the blood from patient P. T. must be specially mentioned. In one, a big yellow guinea-pig, the blood was found absolutely free from parasites on the day before, on the day of injection, and on the two following days. On the fourth day, a number of intracorpuscular bodies were observed, about ten in a thin smear, which showed one or two well-defined red (chromatin) granules and a distinctly blue stained (protoplasmic) body. These elements are shown in Plate II, figs. 16-20. On two subsequent examinations during the following days similar, but less well-defined, elements were observed (Plate II, fig. 21); afterwards they were absent. The other animal was a spotted guinea-pig, in the blood of which elements as in the previous one were found on the fourth and fifth day following injection (Plate II, fig. 23); but well-defined bodies, like those seen on the fourth day in the first animal, were never observed. In both cases similar bodies were also seen in the protoplasm of mononuclear leucocytes (Plate II, fig. 22).

The importance of this experimental result should not be overrated, as it stands isolated. The sharp definition of the bodies observed makes it, on the other hand, impossible to pass it over in silence. The bodies, as it is evident from the figures, give distinctly the impression of parasites; they are very similar to *Babesia*, especially the two ring forms. In fact, I feel sure that their parasitic nature would never be questioned if they had been observed in cow's blood. Their resemblance to *P. flavigenum* is also very great, though the ring in fig. 18 appears somewhat large in comparison with the ring forms observed in yellow fever blood. The most pertinent question is, whether it is possible that we may have to do with a parasite casually found in the guinea-pig's blood. These animals are not frequently found infected with *Babesia*, but such parasites have been described by Baldrey (1910 and 1911).

It is remarkable that these apparently parasitic elements have been observed only after injection with yellow fever blood, and also, that they soon disappeared again. The question may be raised whether the bodies might simply be yellow fever parasites surviving in the human blood corpuscles which had been injected; this, however, seems very unlikely, as the blood corpuscles were fairly well preserved, which would probably not have been the case with human erythrocytes four days after their injection into an animal of a different species.

An explanation which seems more likely to be correct, than any other, is that some yellow fever parasites have been able to survive for some time in the guinea-pig's blood, have reproduced, and invaded erythrocytes, but have been unable to thrive for any length of time in a medium, to which they have not been accustomed, and have therefore finally died out. Thus we would also interpret the presence of the apparently degenerating elements, which were observed for some days in the blood of the two guinea-pigs.

The blood of several other guinea-pigs examined contained metachromatic erythrocytes, erythrocytes with nuclear remains, and erythroblasts, but in no case elements which could be mistaken for those here described.

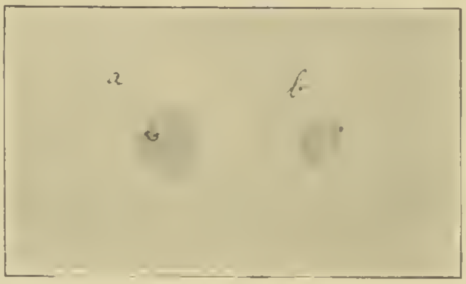
IX. EXPERIMENTS WITH MOSQUITOS

The conditions for successful mosquito experiments were not favourable. Most patients were admitted to the lazaret in a late stage of the disease, and I wanted to work with mosquitos infected during the first few days, in order to have the greatest possible chance for obtaining positive results. When a patient had been admitted, I could think of no experimental work before the diagnosis of yellow fever had been confirmed officially. Next, I had to obtain permission for experimenting, and to persuade patients to submit to mosquito bites. Several patients did so, but not very willingly, and the nurses were decidedly opposed to these experiments. I must confess also that it is with some reluctance that I ask a patient to submit to the application of mosquitos. So far, at least, have modern theories become diffused that this request, to a somewhat intelligent individual, intimates a knowledge of his diagnosis, which one does not often care to tell a yellow fever patient until after his recovery. Finally, my time was mostly taken up with the direct examination of the blood, which part of my work I considered more urgent than any other. The result was that only a few experiments were made, and not a single one completed exactly as I had proposed.

The object of my mosquito experiments was not to infect other individuals, but only to investigate the fate of *P. flavigenum* when taken up by the mosquito. For this purpose I proposed to infect a number of mosquitos, causing them to suck blood from yellow fever patients in an early stage of the disease, and afterwards kill one or several on each subsequent day up to the fifteenth. I would then examine, in fresh and stained preparations, stomach and salivary glands, and make sections of mosquitos embedded in paraffin.

This programme was not carried out. I obtained only in two cases a fair number of *S. fasciata* ♀ (22 in one case, and 30-40 in another) which had fed on the patients O. R. and L.P., on the sixth and third day of their illness, respectively. Several mosquitos were examined the following days, stomachs and salivary glands dissected, fresh specimens observed with ordinary illumination and with paraboloid condenser, and fixed preparations stained after Giemsa and with iron-haematein; but no result was obtained. The last mosquitos were examined on the eighth day in the one case, and on the twelfth in the other, as a number of them died. Several mosquitos which were supposed to have fed on patients and a number of fresh mosquitos were also examined, and a material for comparison, which may be of use in future work, was thus obtained.

The only elements which possibly may be of interest were found in the stomach contents of a mosquito which had fed on O. R., and was killed on the following day (text fig. VII). I cannot say anything about their nature.



Text Fig. VII.

From stomach contents of *S. fasciata*, 20 hrs. after infection : *a*, erythrocyte containing two parasites ; *b*, free body.

These negative results were somewhat discouraging. But, considering the delicate technique of such investigations, and the very imperfect way in which they were carried out, they cannot be taken as a demonstration that positive results cannot be obtained by continued work on this line.

X. PATHOLOGICAL OBSERVATIONS

No special pathological study was undertaken. The lesions observed at the post-mortem table and by microscopical examination were the same which I have discussed in my paper on post-mortem diagnosis (1911, 4). In the foregoing sections several notes from autopsies are given (pp. 136, 148, 164, and 172). A few blood counts were made in the earlier cases, but, as this material is very scarce, it is reserved for later publication together with further observations. It is also the intention to publish at a later date the results of experiments which were undertaken with the object of making a comparative study of the pathogenesis of jaundice, producing phosphorus poisoning in rabbits.

XI. COMPLEMENT DEVIATION

This diagnostic method has, as far as I am aware, not been used in yellow fever. My own experience with this test is limited to three cases. In each case the reaction was carried out, simultaneously, with yellow fever serum and yellow fever antigen, yellow fever serum and syphilitic antigen, and syphilitic serum and syphilitic antigen. The blood was always taken by venepuncture, and the serum inactivated; as yellow fever antigen an extract of yellow fever liver was used, and, in one case, of yellow fever myocardium besides; the syphilis antigen was extract of human (normal) myocardium. The organic extracts were prepared with 96 % alcohol. All dilutions were made with 0·85 % Na Cl sol. The following scheme shows the technique, complement and amboceptor having been estimated previously (all measures in c.c.):—

Test Tube No.	Antigen	Specific serum	Complement (Fresh guinea-pig serum)	Amboceptor (serum of rabbit immunized against sheep's erythrocytes) sol. 1:200 or 1:1000	Suspension of sheep's erythrocytes (5%)	NaCl sol. (0·85%)
I (control) ..	0	0·2	0·1	1	1	2·7
II	0·2	0·2	0·1	1	1	2·5
III	0·2	0·1	0·1	1	1	2·6
IV	0·2	0·05	0·1	1	1	2·65
V (control) ..	0·2	0	0·1	1	1	2·7

The test was made in the cases O. R., A. D., and H. S., in the first case during the illness, in the second once during the illness and once after recovery, and in the third twice after recovery. The serum of O.R. produced deviation both with yellow fever and with syphilis antigen, the sera of A. D. and H. S. with neither. It is, therefore, reasonable to suppose that the reaction in the case of O. R. was due to a previous syphilitic infection, of which no history was obtained, but to which the patient, a Mexican soldier of 35 years, may, very likely, have been exposed. Syphilitic serum would be expected to react both with extract of normal myocardium and of yellow fever liver, perhaps showing a quantitative difference; in the case of O. R. the intensity of the reaction was practically the same with both extracts. With regard to serum of yellow fever patients, or convalescents, one might possibly have expected that it would react with specific liver extract, but not with other organic extracts; this, however, seems not to be the case, according to my observations.

XII. NOTES ON TREATMENT

In my previous paper on the treatment of yellow fever cases (1911, 2), I mentioned the possibility of using salvarsan in this disease. Soon after, Professor Ehrlich wrote to me approving this suggestion and offering his assistance. Since then a paper by Pareja (1911) has appeared, in which the author states he has tried salvarsan treatment in yellow fever cases, with no favourable results.

I am very much indebted to His Excellency Geheimrat Ehrlich for his good advice, and for the abundant supply of salvarsan which he sent me to Mérida. I was very anxious to try the treatment with salvarsan, which, from a theoretical point of view, undoubtedly seems rational in the case of yellow fever. Salvarsan has been proved to be a powerful parasiticidal agent in various protozoal infections, and it is obvious that we need an efficient—and harmless—agent of that kind in yellow fever. The use of salvarsan in malaria, however, has not been very encouraging; and in yellow fever it might possibly do harm on account of the very common and severe kidney affections, though in syphilis such affections do not seem to constitute a formal contra-indication against the use of salvarsan. Professor Ehrlich advised me to inject first a small dose, and shortly after repeat the injection should no untoward symptoms present themselves. He also emphasizes that the water should be distilled immediately before use, in view of the recently demonstrated fact that distilled water, though sterilized, may produce symptoms of poisoning if it contains dead remains of bacteria.

In an acute disease, as yellow fever, it seemed obvious that intramuscular and subcutaneous injections could not be trusted. Only when introduced directly into the circulation, might salvarsan be expected to have a sufficiently powerful effect. The cases to be experimented with should be carefully selected; in extremely severe cases a new remedy should not be tried, as a fatal issue in such would probably be unavoidable. On the other hand, in mild cases one would not like to employ a toxic substance which might possibly, in spite of all precautions, prove harmful; besides, in mild cases it would prove nothing if recovery took place after administration of a certain remedy, as the same result might be expected to follow spontaneously. For one or other of these reasons most of the cases seen in Mérida were rejected as unsuitable for salvarsan treatment; it may be said also that, if I was anxious to try the effect of salvarsan in yellow fever cases, most of my colleagues in Mérida were by no means so. Finally, the case of A. D. was selected. In this case the infection was evidently very severe; haemorrhagic symptoms had been pronounced, and seemed to be increasing again at the time when patient was admitted to the lazaret. The kidneys were evidently severely affected. I have already referred to this case as conveying the impression that there was a sort of recrudescence on the sixth day of disease. The only circumstance which gave me a slight hope that this patient might be saved, was that the amount of urine was on the increase. With Dr. Vargas's authorization I undertook his treatment. The clinical history is the following:—

March 17, 1912.—A. D., 21 years, male, Spaniard (Canary Islands). (Chart XIV).

Patient felt ill on March 11, in the morning, with fever and headache. On the 12th the temperature was 40·3° C. in the morning and 39° C. in the afternoon. There was nausea and vomiting, to begin with of ingested food, afterwards greenish and, during the following night black, haemorrhagic. Melaena. On the 14th the urine was very dark, and on the 16th he passed no urine at all.

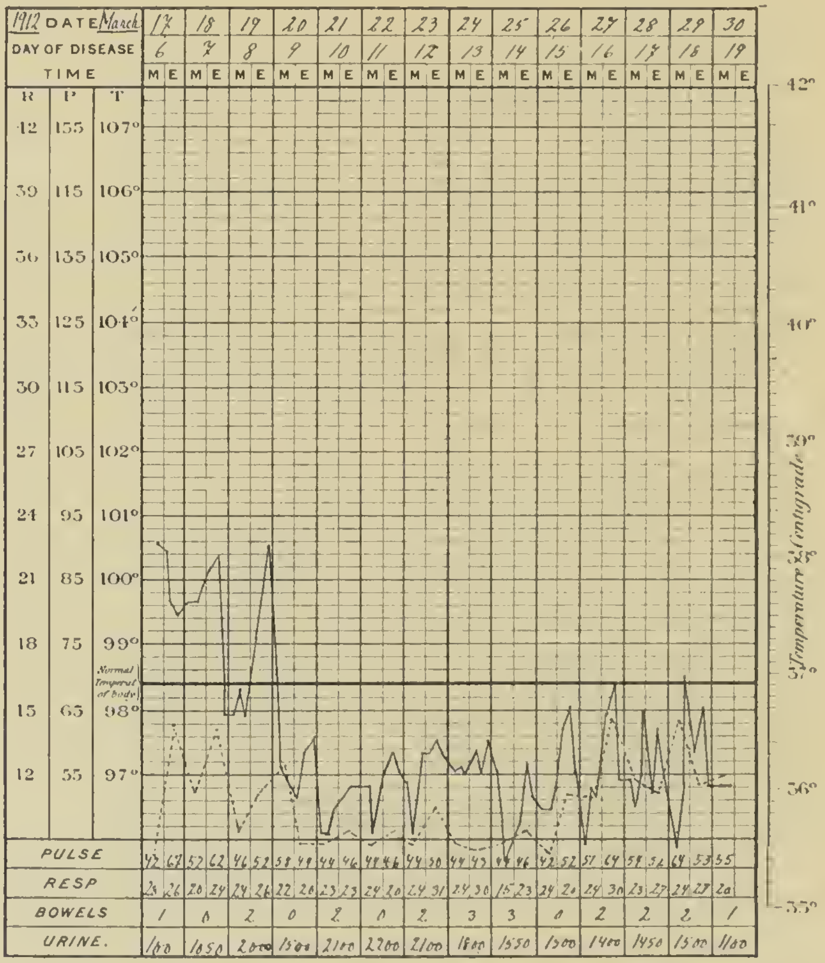


CHART XIV.

On admission patient complains of headache, rachialgia, especially lumbar and epigastric pain, which increases on pressure. There is intense general jaundice and conjunctival hyperaemia. Tongue coated, with hyperaemic borders.

March 18.—Insomnia, delirium and agitation. Intense thirst. Pulse soft and weak. Stimulantia.

March 19.—Delirium less pronounced. Jaundice increased. Tongue and gums with haemorrhages. Vomit slightly black. At twelve noon, 0·1 gm. Salvarsan is given intravenously, and at 9 p.m. 0·2 gm. No untoward symptoms followed the injections, on the contrary there was observed, in the course of the day, some slight improvement of the general status and of the characters of the pulse. The pulse rate was 48 in the morning, and the pulse very soft. In the afternoon the pulse (60) was considerably stronger; in fact, it seemed to become stronger after each injection.

March 20-22.—Delirium gradually disappearing, as also epigastric pain, backache, and pain in limbs. Headache persists. Sleep improved. Melaena after purgen tablet and enema.

March 23-28.—Jaundice gradually diminishing. Patient gaining strength.

March 30.—Patient transferred to hospital, apparently well, but still with albuminuria and jaundice.

The *blood* contained *P. flavigenum*, but no malarial parasites.

Urine: sp. gr. 1·015. Albumin 0·75 °/₀₀. Faint indican reaction. Faint reaction for bile pigments, and very faint for urobilin. Diazo reaction negative. Numerous granular casts. No leucocytes, nor erythrocytes. Few renal and duct epithelia. Numerous fat granules.

This case was officially diagnosed as yellow fever on March 18.

It was decidedly my impression that the patient improved after the injections, but, of course, from one case no conclusion can be drawn. With regard to the question of any harmful effect of salvarsan, no such effect was evident. The temperature rose after the first injection, in the course of about six hours, to 38·1° C., but soon went down again. The albuminuria was more persistent in this case than is the rule in yellow fever, but, should this phenomenon have been due to salvarsan, the damage done to the kidneys was, at any rate, not serious; a few weeks later the urine was examined, and normal characters found.

On the whole, I was somewhat surprised that this patient recovered. But similar surprises occur also in cases treated without salvarsan, as the following clinical history may serve to illustrate.

February 7, 1912.—O. R., 35 years, male, Mexican (from Jaltan, Querétaro, yellow fever-free place). Patient complains on admission of slight backache and pain in limbs.

February 8.—Face congested. Conjunctival hyperaemia. Light scleral jaundice. Tongue coated, with red borders. Slight haemorrhage from gums. Epigastric pain. Nausea; vomits, remains of food, mucus, bile, and, in the afternoon, black vomit. At the same time gingival haemorrhages increase. Headache; backache more pronounced than yesterday. Agitation.

February 9.—Gingival haemorrhage. Black vomit. Melaena. Jaundice. The following day there was no change in patient's condition; the 11th, there was no black vomit, and less haemorrhage from the gums. From the 12th jaundice began to decrease, on the 13th general improvement was noticed and from that date recovery was uninterrupted. The temperatures from February 12 to February 20 oscillated between 35·5 and 36·5, the pulse between 44 and 52. The daily amount of urine increased to about 1900 c.c.

February 20.—Patient leaves hospital.

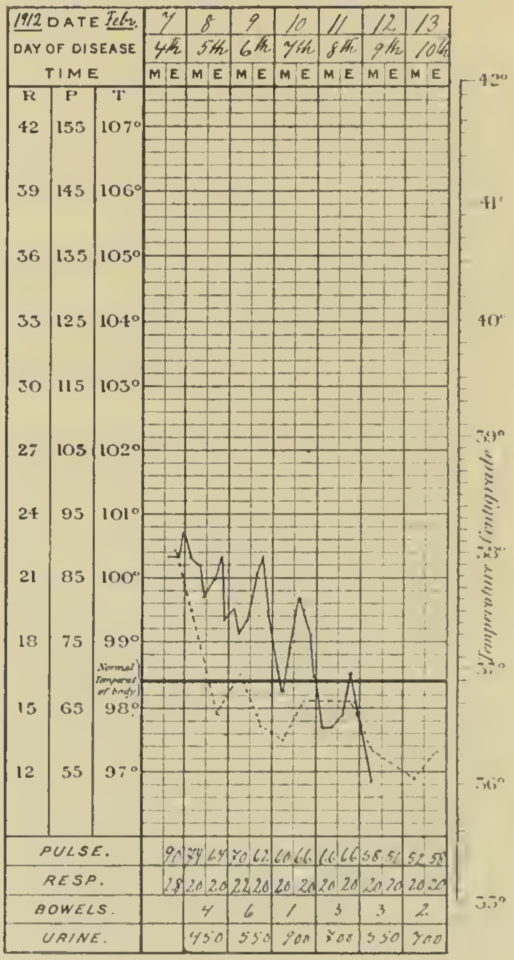


Chart XV.

In the *blood P. flavigenum* was found, but no malarial parasites.

Urine.—February 10, sp. gr. 1·030, albumin: 0·75°/₀₀. Indican reaction positive. Diazo reaction negative. A few granular casts and renal epithelia.

February 17.—No albumin. No casts. No renal cells. Indican reaction very intense. Diazo reaction negative. Urobilin: faint reaction. Bilirubin: intense reaction.

This case was officially diagnosed as yellow fever on February 10.

The treatment in this case was essentially the same which I have recommended in my earlier paper (1911, 2).

The very doubtful prognosis in most cases of yellow fever makes it very difficult to arrive at a definite conclusion with regard to the value of any treatment.

XIII. MOSQUITO SURVEY

Dr. Casares and, later on, Dr. Rojas arranged that their sanitary inspectors should collect daily ten or twelve bottles with mosquito larvae, from different houses. The bottles were sent to me the same or the following day, and I made once or twice weekly a rough classification, estimating separately the number of larvae of *Stegomyia* and of those of other *Culicinae;* larvae of *Anophelinae* were never found, and only exceptionally rarer mosquitos, as on one occasion a single larva of *Megarhinus sp.* (*splendens*?).

In this way no intimate knowledge was obtained of the mosquitos of Mérida, but much valuable information with regard to two points of the greatest epidemiological importance, namely the distribution of mosquito breeding-places, and the prevalence of *S. fasciata.* Larvae were obtained from 750 houses from different, though not from all, parts of the city. I have no means of determining the proportion between the number of houses inspected, and those in which larvae were found, as the inspectors could not, for practical reasons, collect samples from all places where they found larvae. But there is no doubt that larvae-free houses were in a conspicuous minority. In 592 out of the 750 samples, *Stegomyia* larvae were alone present, in 26 larvae of other *Culicinae*, but no *Stegomyia*, and in 132 both *Stegomyia* larvae and larvae of other *Culicinae.* Thus, *Stegomyia*—and in all cases in which the larvae hatched, *S. fasciata* developed—was present in, at least, 724 houses out of 750 in which larvae were found. The sketch on Map IV will convey an idea of the distribution of the *Stegomyia* infested houses, but it must be emphasized that the distribution here shown represents a minimum, very much inferior to the real conditions; I feel certain that a complete and repeated survey would show that all houses, with very few exceptions, are infested with mosquitos, and mosquitos are in Mérida, in at least 80 per cent. of cases, *Stegomyia*. It is an important feature that *Stegomyia* were just as common in the central parts of the city as in the suburbs. The numbers of larvae contained in samples varied from one or two to several thousands.

I received also larvae from various smaller towns and country districts, and made personal observations in others.

In Maxcanú, where we saw a patient with yellow fever, we caught a few *Stegomyia fasciata* and *Culex sp.* in the sick-room, but no larvae were discovered, though house and garden were thoroughly searched. On the other hand, a sewage well in the Municipal Building of this town contained numerous *Stegomyia* larvae.

In Temax and in Motul, *Stegomyia* larvae were found in Municipal Buildings, churches, and private houses.

In Progreso I have seen *S. fasciata* on several occasions, and this mosquito is said to be common, as well as other mosquitos.

In Izamal I found *S. fasciata*, and Dr. Arzápalo told me that it was very common.

On the hacienda Chablé numerous larvae were found, *Culex sp.* in water-troughs for cattle, and *S. fasciata* in rainwater containers.

On the hacienda Citincabchén only few larvae were found of *S. fasciata*, *Culex sp.*, and *Aedes sp.*

On the hacienda Kambul larvae and adults of *S. fasciata* and *Culex sp.* were found. A sample from the ranch Kulinché contained *Culex* larvae.

Samples of water from the hacienda Kokochacaj contained *Culex* larvae.

The water containers, in which larvae were found, varied from wells and tanks to bottles, tin cans, and other small receptacles which had been left in odd places, or thrown away, and contained a small quantity of water.

Old barrels, in the bottom of which a little rain water had collected, were frequent breeding-places. Containers, which were emptied daily, were repeatedly found to contain larvae; a few drops of water had been left at the bottom when they were emptied. Water, containing a considerable amount of charcoal ashes, is stored for washing purposes in almost every house in Mérida. It is a common belief that mosquito larvae do not thrive in this lye, but observation has not borne out this contention; on the contrary, they are frequently found in enormous number.

The holy water receptacles were fairly well kept in most churches in Mérida, as Dr. Casares had already at some earlier time called attention to this matter. An inspection, by Dr. Casares and myself, of thirteen churches in Mérida resulted in the finding of *Stegomyia* larvae in 3 out of 26 receptacles examined. But in the churches in smaller towns the holy water was often swarming with larvae.

Many inhabitants of Mérida had the idea that the sewage wells at the street crossings were important breeding-places for mosquitos, but this I do not believe to be the case. They are petrolized at six or seven days' interval, and, it appeared, in an efficient manner. I inspected a number of these wells with Dr. Casares and his petrolizing squad, but in no case did I see mosquitos escaping from the wells when opened.

It appears strange that mosquitos still are so extremely numerous in spite of the campaign which has been waged against them for years. The general impression of people living in Mérida is that mosquitos are just as abundant at the present time as they were ten years ago. There are no swamps which can be held responsible, nor do I think, as I have just said, that the public sewage wells are of any importance as breeding-places. The principal, if not the only, breeding-places are evidently water containers in private houses; also private sewage wells, which are not properly and regularly petrolized, are commonly infested with mosquitos. The sanitary regulations impose the obligation on the inhabitants of keeping all tanks covered in a mosquito-proof way, but this obligation is not complied with, and is, in fact, very difficult to enforce. Most houses have tanks for the storage of both rain water and well water, and the expense of purchase and maintenance of mosquito-proof covers is not inconsiderable, especially as it is exacted that they shall be made according to a given model. Odd receptacles are still very common in Mérida, and I think they are even more important as breeding-places than the tanks. But, whilst it may be possible to get rid of odd receptacles by a more frequent inspection, it will remain a difficult problem how to deal with water tanks and private sewage wells, as long as Mérida is not in possession of a central water supply and a proper sewage system; these reforms seem, however, far off. Thus it will be necessary, for years to come, to carry on the anti-mosquito campaign on similar lines as hitherto, though, it is to be hoped, in a more efficient way, and with better results.

In addition to these notes on the prevalence of mosquitos in Yucatán, it may be of interest to mention an observation which I made on my return voyage from Progreso to New York. In Habana a large quantity of pineapples were taken on board—I believe 20,000 boxes—in fact, they formed almost the whole cargo. One morning, on the second day after we had left Habana, the Chief Officer woke me with the notice that we had mosquitos on board. During the whole of that day and the following night they were found in large numbers on the deck and in the Captain's cabin. We were far from land, so I suspected we must have carried the mosquitos from Habana, and went down into the holds with the Chief Officer, where we found mosquitos in enormous numbers amongst the pineapples. I caught a number of mosquitos, but did not get them home in sufficiently good shape to have them identified; two only I identified on the spot as *S. fasciata*, but I did not see any more of that species. This observation is of interest in showing to how large an extent ships may serve as mosquito carriers. It must be quite exceptional that mosquitos are observed on the deck of a steamship at sea, as they will, in most cases, be blown away. In this case we had absolutely calm weather on deck; the smoke from the funnel went straight upwards, so there must have been a faint breeze blowing in the same direction as the ship was sailing, and with the same speed. The ship's officers told me that they had never before seen mosquitos on deck. As a rule some mosquitos will undoubtedly be blown away during the voyage, but the majority will in all probability remain in the holds and escape at the port of arrival. Fortunately, pineapples and other fruit do not come from severely infected areas, which are the populated centres; the mosquitos contained amongst them are not likely to be *Stegomyia*, and if they were, they would very likely not be infected.

A number of mosquitos were brought home from Yucatán and given over to Professor R. Newstead, who will report on them later on.

XIV. NOTES ON MOSQUITOS AND MOSQUITO EXTERMINATION

I

The theory that yellow fever is transmitted by mosquitos biting at night time is supported by epidemiological facts, particularly by the observation that, during the endemic reign of yellow fever in Rio de Janeiro, foreigners escaped infection when they retired to Petropolis during the night (Azevedo Sodré and Couto, 1901), and by the experimental results of Marchoux and Simond (1906). But biological observation of *S. fasciata* is not very much in accordance with this theory, and an ingenious explanation has become necessary to solve the difficulty thus arising (Marchoux and Simond, *loc. cit.*)

Carroll (1905) speaks of the twilight habits of *S. fasciata*, but most other observers mention the day-biting habits of this mosquito, or simply refer to it as a daylight mosquito (Finlay (1886), Durham (1902), Goeldi (1905), Boyce (1911), McCoy (1912), and others). I have repeatedly stated my experience that *S. fasciata* bites indiscriminately at day and at night time, and I have now again found this experience confirmed. In the laboratory, where *Stegomyiae* were prevalent, but no other mosquitos ever found, I was bitten at any time of the day, and I have repeatedly watched *Stegomyia* females sucking on my arm and filling themselves at 10 and 11 o'clock in the forenoon. On the other hand, in my room at the hotel (second floor of a very high building), where I never saw any *Stegomyia*, but numerous *Culex*, I was never bitten in the morning, nor in the afternoon, but frequently in the late evening. I have not observed this time, as previously, any marked difference in the biting habits of *S. fasciata* between the forenoon and late afternoon hours (from 3 to 6), but I believe my earlier statement to be correct, as it referred to observations made during a much longer period, and at all seasons of the year.

II

The question of the most efficient and most practical method of mosquito extermination is one of very great importance. Such methods as filling in and draining, which play a great rôle in anti-malarial campaigns, are of comparatively little value when dealing with yellow fever. They should, however, be carried out whenever possible, and may occasionally be useful in a campaign against yellow fever in the country, as small pools sometimes harbour *Stegomyia* larvae. But in the majority of cases we have to deal with destruction of larvae and adult mosquitos in houses.

The principal method of larvae destruction is petrolization. This method is by all authors considered efficient, but there is considerable divergence as to the quantity of oil recommended per unit of surface, a question of no slight economical importance. Boyce (1911) recommends 1 oz. of oil to the square superficial yard, i.e., slightly over 30 grams to the square metre, but Simond (1912) advises 150 grams to the square metre of surface. I have found the amount recommended by Boyce sufficient on a quiet surface, but would in practice advise the use of somewhat larger quantities.

Using 3 c.c. of refined petroleum on a surface of 90 c.c. (10 l. of water containing *Stegomyia* larvae), I found that all larvae eventually died, but the time of survival varied considerably. Sometimes all died in less than two hours, but in one experiment I found several larvae surviving for fourteen hours, and one for more than sixteen.

A 'mosquito oil,' the composition of which I do not know, but which was sent me for experimental purposes by Messrs. Meade-King and Robinson, of Liverpool, did not spread so uniformly on the surface of water as refined petroleum did. When it was applied according to the same method as above, all larvae finally died, but some survived for a somewhat longer time than in the experiments with petroleum. Once I saw a single larva surviving for about twenty hours, all others having succumbed many hours before.

This exceptional survival of single larvae is an interesting phenomenon. Mosquito larvae ordinarily rise to the surface with short intervals, but when forcibly excluded from access to air, some are able to continue their existence for a surprisingly long time without breathing. In the above case there may have been, for several hours until the 'mosquito oil' had formed a uniform layer, a possibility of reaching an uncovered portion of the surface, but I feel convinced that the larva has lived for at least twelve hours without breathing. During one hour, the fifteenth after addition of 'mosquito oil,' I observed the larva uninterruptedly, and saw it moving about in the deeper parts of the water, without even attempting to reach the surface.

Chemical poisons, dissolving in water, have been recommended as larvicides by various authors. Petroleum has, undoubtedly, some inconveniences, but it appears to me that those of chemical poisons are, as a rule, greater. I have experimented with several poisons in watery solutions, and have found a very high degree of resistance against their effect in the case of larvae of *S. fasciata*.

A. Mercury bichloride. A solution of 1 : 10,000 had very little effect, killing only a few of the larvae, even in the course of twenty hours. A solution of 1 : 1000 killed all larvae in from six to twelve hours, but most pupae survived, and some were seen developing into imagines.

B. Sol. lysoli. 1 : 400 killed larvae in fifteen minutes, pupae in two and a half hours.

C. Sol. hypermanganatis kalici, 1 : 500. All larvae living after four hours.

D. Potassium cyanide. 1 : 10,000 killed larvae in one and a half hours, 1 : 100,000 most larvae in four to five hours; but in the latter case a few survived more than twenty-four hours, and most pupae survived even longer, whilst several developed into imagines. In a solution 1 : 133,000 of this substance, all larvae were alive after three hours, about 20% alive after twenty-five hours, and all pupae were at this time either alive or had developed into imagines. A solution of 1 : 200,000 killed less than 10% of larvae in forty-eight hours.

These results with potassium cyanide are somewhat inferior to those obtained by Ross and Edie (1911), who experimented with larvae of *Culex pipiens*. I obtained no results with the potassium cyanide and soap tablets, recommended by these authors, and sent to me by Messrs. Meade-King and Robinson. All larvae remained alive, even after three days, in 10 l. water, to which one tablet had been added. I suppose the potassium cyanide decomposes when dissolved in water together with the soap, as it could be demonstrated neither in the water nor in the tablet when this had been floating in water for two hours, though the powder contained in the tablet gave the characteristic smell and reactions for potassium cyanide when the tablet was opened dry.

A strong current of light gas was passed through a small quantity of water containing mosquito larvae for several minutes without killing them.

In the case of water tanks, oiling is inadmissible and complete closure not convenient. Screening then becomes necessary, and for this purpose strong wire-gauze, sixteen meshes per inch, should be used. In water kept for ornamental purposes larvae-eating fish are stocked.

For destruction of adult mosquitos fumigation with sulphur remains the method in common use. I have recently (1912, 1) discussed the advantages and disadvantages of this method, and need only repeat here that it is highly desirable to find another method, which is at the same time efficient and has no untoward effect upon delicate objects and on foodstuffs.

With this object in view I made a number of experiments with light gas. In laboratory experiments, on a small scale, this gas gave excellent results. A stream of gas, introduced into a bottle or other small container, killed all mosquitos. When I had convinced myself of this result, I proceeded to experiments on a larger scale, which I undertook, with the assistance of Dr. Casares, in a room in the lazaret. This room, of about 50 cubic metres, was prepared as if for sulphur fumigation, and test mosquitos were distributed in the room. The mosquitos were contained in three or four cages, of which one was put on the floor, one on a table, one was hung near the top of the window, and one, in some experiments, near the centre of the ceiling. The gas was introduced through a rubber tube which was connected with a pipe in an adjoining room, and passed through an opening which had been bored in the door. The first experiment, in which the gas-pipe was left open for an hour, gave a negative result.

In the second experiment the gas was left open for two hours, and 110 cubic feet were used; thereafter the room was kept closed for about thirteen hours, after which time the mosquitos were found dead. Subsequent experiments, however, showed that in order to obtain satisfactory results much larger quantities of gas had to be used. Using four hours of gas current, and four hours' exposure afterwards, all mosquitos in the cages were apparently dead, but only those from the upper part of the room remained so, whilst some in the cage which had been standing on the table, and most in that from the floor, revived quickly after having been brought into fresh air. Likewise, after six hours' gas current, and two hours' subsequent exposure, many mosquitos in the lower cages were only stupefied. Finally, after six hours' gas current, and twenty-three hours' total exposure all mosquitos were dead.

It was my intention to continue these experiments, but it seems now possible that fumigation with cresyl, as recommended by Bouet and Roubaud (1912), will prove so advantageous that the experiments with gas may be discontinued.

A few words should be added about the wire-gauze used for screening. The material (oxidized phosphor-bronze) recommended by Melville-Davison (1911) was used for screening the guinea-pigs' department, and seemed to stand the climate perfectly well; but, as the time of observation was very short, I expect to receive information on this matter, later on, from Dr. Hernandez.

In the paper referred to, Melville-Davison recommends the gauze which has sixteen meshes per inch, but suggests the possibility of increasing the size of the mesh to 14 x 14. This is a question of great practical importance, as the latter size undoubtedly allows the passage of more air, and Dr. Davison informs me that there has been some complaint from ships' crews on account of poor ventilation through wire-gauze with narrow meshes (16 x 16). But, of course, safety should not be sacrificed. I therefore tried the two kinds of wire-gauze with *S. fasciata*. They were kept back by the gauze with 16 x 16 meshes, but not by the 14 x 14 gauze. A cage of 14 x 14 gauze, containing numerous *S. fasciata*, but neither food nor water, was placed inside a larger cage of 16 x 16 gauze containing water and fruit, but no mosquitos; several mosquitos passed out from the inner into the outer cage in the course of five to six hours, and nearly all in twenty-four hours. In practice, conditions may be slightly different, but I cannot recommend the 14 x 14 wire-gauze as a safe protection against *S. fasciata*.

XV. *LEISHMANIASIS CUTANEA*

I had, for a long time, been on the look-out for the various forms of tropical ulcers, but failed to find any of a specific nature, until Mr. Th. Maler, an Austrian archaeologist, who has lived for nearly fifty years in Yucatán, told me about a peculiar affection which he had observed with great frequency during his travels in the interior. He said that the 'chicleros,' Indian labourers who collect chicle (the raw material of chewing-gum), suffered severely from a certain kind of ulcer, which always started on the external ear, often destroying it completely, and invading the face to a large extent. The natives did not, as a rule, apply for treatment, and, even if they did, favourable results were but seldom obtained. Mr. Maler, however, claimed to obtain a perfect cure in a short time by a single application of pure liquid carbolic acid by means of a brush.

On making inquiries among the local physicians, I found that this disease was, apparently, very little known, but after a short time, Dr. L. Guzman was able to send me two cases. Both were young natives, chicleros, and in both cases extensive ulcers were present on the upper part of the helix of one ear, with somewhat elevated, irregular borders, granular surface beset with minute vesicles, considerable destruction of the tissues, and beginning deformation due to cicatricial retraction. In one case, there was also a non-ulcerated nodule, of semi-soft consistence, on the cheek. When these cases were demonstrated, several colleagues, who had practised in the country districts, declared they knew the disease quite well; in fact, one practitioner, Dr. M. Canto, remembered to have seen, years ago, about 150 cases in the course of a few years. The disease is evidently met with in all parts of the peninsula, both in the interior of Yucatán, in Campeche and in Quintana Roo. Also many laymen knew the affection as a typical one, the 'ear ulcer of the chicleros.'

Later on, four other cases, evidently of the same nature, came under my observation. In all cases ulcers were present on the ear, and in two of them additional ulcers, in one on the forearm, and in the other on the leg. In the former of these two cases, the patient explained that he used to rest his head on his arm when sleeping in his hammock, in such a way that the ulcerated portion of the ear would come in contact with that particular place of the forearm where the ulcer had formed secondarily. The patients could give no exact data as to the duration of the ulcers, but, in most cases, they had been aware of their existence for several months.

In all cases, smears were made from the ulcers, and, in the first case, from the nodule on the cheek. In four cases *Leishmaniae* were found, mostly in small numbers, but in the liquid which was obtained from the closed nodule the parasites were fairly numerous. In one case a first examination proved negative, but a few days later parasites were found. In the two negative cases I had no opportunity of repeating the examination, but, in view of the clinical features, I must consider the ulcers in these two cases identical with those in which parasites were found.

In addition to these cases, I saw one in which the diagnosis remained doubtful. The patient was an elderly man, who had been working in the woods, and had suffered for some time from an ulcer on the ear, which had, however, healed almost completely when I saw him. At that time he had an ulcerated nodule on the back of the wrist. This nodule was punctured, and smears prepared, but no parasites could be found.

The affection had lasted, in the six cases, from two to eight months, but in severe cases the ulcers were said to persist for about two years.

It is a common belief in Yucatán that the disease is transmitted from one individual to another by means of some insect; in one part of the country a 'white mosquito' is said to act as transmitter, in another district a black fly is suspected, and several laymen suggested to me the possibility of indirect transmission. They believed that a parasite of flies, probably a *Trombidium*, might infect itself on a patient, and then be transported to a healthy individual.

The treatment with pure carbolic acid, as recommended by

Mr. Maler, was applied in several cases; these patients improved rapidly, though the parasites did not disappear; on the contrary, in one case, the parasites were very scarce at the first examination, but fairly numerous two or three weeks later, though at that time the ulcer had a much cleaner aspect than when seen for the first time.

The parasites observed had the morphological characters of *Leishmania tropica* (Plate III, figs. 1 and 2); they were mostly situated inside large mononuclear cells, from two or three to about twenty in a single cell.

A peculiar feature was that in the four cases in which the *Leishmania* was found, a characteristic diplococcus was also observed. In two cases secondary infection was evident, many different bacteria being present in the smears, but in the other two cases the diplococcus was the only associated microbe. One of the latter cases was that of the young man with a non-ulcerated nodule on his cheek. The skin over this nodule was apparently intact, and nothing suggested that a secondary infection might have occurred. Similar diplococci were also found in one of the cases, in which no *Leishmania* were observed. I feel inclined, therefore, to regard this coccus as primarily associated with the *Leishmania*, in which case it would probably be of pathogenic importance.

The diplococcus (Plate III, figs. 3, 4 and 5) was free, or enclosed in polymorphonuclear leucocytes, or in large mononuclear cells; it showed considerable resemblance to the gonococcus, morphologically, but retained the colour by the Gram-process. No culture was obtained on ordinary media.

Dermal leishmaniasis has repeatedly been observed in the New World. From Brazil it has been described by Lindenberg (1909), Carini and Paranhos (1909), Splendore (1911) (mucous membranes), and Werner (1911); from French Guiana by Nattan-Larrier, Touin, and Heckenroth (1909); from Dutch Guiana (Surinam) by Flu (1911); and from Panama by Darling (1910, 1911) and Darling and Connor (1911). The case described by Darling and Connor is the only one in which the same localisation on the external ear was observed, which seems to be so characteristic for the affection, as seen in Yucatán. In fact, the photographs given by these authors show very much the same characters which I have observed in the cases here reported. The other peculiar feature which I found in my cases, the association of the *Leishmania tropica* with a characteristic diplococcus, is not mentioned in the descriptions referred to.

XVI. BABESIASIS

In an earlier paper (1912, 2) I mentioned an acute, febrile disease, which is observed in Yucatán in imported cattle, and known by the name of 'yellow fever.' The symptoms are similar to those of Texas fever. High febrile temperatures, albuminuria, haemoglobinuria, oliguria, anuria, haematemesis and melaena are observed. The disease causes considerable losses: according to an estimate of a cattle-importer, it would kill in three months cattle valued at about $70,000 Mex. (£7,000). Very little or nothing is done to combat the disease.

Native cattle are said to suffer from the disease in a mild form, especially the calves.

I saw seven cases of this disease. In six cases I found parasites, which appeared as minute solid elements (Plate III, figs. 11 and 16), ring-forms (figs. 14, 15, 17 and 22), single or double pyriform bodies (figs. 12, 18, 10, 24 and 25), and also the characteristic division forms (fig. 23), described by Nuttall and Graham-Smith (1908). I have not been able to follow the whole development of the parasites, but I think there is no doubt about the diagnosis of *Babesia bigemina*. In several cases the parasites were extremely scarce, at a time when the temperature was very high, and in one case, in which salvarsan was applied without any final result, they continued so until the fourth day of the disease; in this case the cow died on the fifth day, and only on this day the parasites were somewhat numerous in the peripheral blood.

In some films, parasites were both very scarce and extremely small, showing considerable resemblance to *P. flavigenum.*

In the one case in which no parasites were found, the blood was examined on the first day only, of an attack of fever, which did not prove fatal, but during which typical symptoms were observed. It is probable that a repeated examination would have shown the presence of parasites.

The following clinical notes are from a characteristic case of the disease; I am indebted for the notes to the owner of the cow, Mr. J. Espinosa:—

March 4, 1912.—Imported cow, about 8 years old. 15 months in Yucatán. Ill this morning. Temperature 41°-41·5° C. Appetite poor.

March 5.—Temperature 42° C. Takes no food. Sanguinolent mucus from the nose.

March 6.—Temperature 40-40·6°. Urine: red, acid, albumin 3 °/₀₀, haemoglobin: intense reaction; bile pigments: reaction negative, diazo reaction negative; numerous granular casts and epithelial cells, a few erythrocytes, no leucocytes.

On this date I saw the cow, took blood smears, and found *Babesia bigemina.* I recommended the owner to give the cow, as an experiment, an intravenous injection of salvarsan. He accepted my advice, but the injection was evidently not given properly, into the vein, as the liquid, according to description, spread into the tissue.

In two further cases of babesiasis I tried salvarsan treatment, administering personally the intravenous injections. In one case nearly two grammes were given, in the other little more than one gramme, as the cow could not be kept quiet during the injection. No untoward effect of the injections was observed, but the disease ran its course, and both cows eventually died.

In a dog, I found a number of very small *Babesia*-like parasites (Plate III, figs. 27-31), and, after searching several smears, the typical double form shown in Plate III, fig. 26. This dog did not suffer from any acute, febrile disease, nor was red urine observed. It suffered from a chronic cachexia.

XVII. ANTHRAX

Lobado is the name of a disease which occurs epidemically amongst cattle in Yucatán, and causes very considerable losses. I examined several times blood from cattle, which had died from this disease, and found by microscopical examination and in cultures a bacterium which seemed morphologically identical with *B. anthracis* and developed, in cultures, very similarly, liquefying gelatine. There appeared to be, however, some differences in the results of experimental inoculation, wherefore a further investigation will have to be undertaken before a final report can be given.

XVIII. HEPATITIS EMPHYSEMATOSA

The following interesting case occurred which I was called to see with Dr. Ayuso:—

Autopsy no. 1144, on body of patient, who died ten minutes after having been admitted to the lazaret.

Principal results: Entero-colitis haemorrhagica et ulcerosa. Hepatitis emphysematosa. Nephritis parenchymatosa acuta duplex. Pneumonia lobi superioris dextri.

Spleen of normal size and consistence, but of slightly darker colour than normally.

Smears from liver show very numerous, from spleen and lung few coarse, straight bacteria. They stained easily by ordinary methods and were Gram-positive (Claudius's method).

Aerobic and anaerobic cultures were made from the liver. In the former no bacteria pathogenic for guinea-pigs developed, but anaerobic cultures (24 hours, at 37·5° C.) killed a guinea-pig in 22 hours by subcutaneous, and another in about 24 hours by intraperitoneal injection. Subcutaneous injection resulted in diffuse and abundant oedematous infiltration with sero-sanguinolent liquid, but no formation of gas. The liver was somewhat enlarged, dark and of soft consistence; no gas formation. In the oedematous exudate numerous, and in the liver few, bacteria were found as described above.

Emphysematous hepatitis has been described by a number of observers, amongst whom Welch and Nuttall (1892), Fraenkel (1902), and Westenhoeffer (1902, 1 and 2). The latter observer, whose view has been accepted by most authorities, arrived at the conclusion, that all emphysematous affections in inner organs are due to post-mortem processes, as he has found, in accordance with other observers, that gas-production never takes place in living tissue, but only subsequent to necrosis. He holds a similar view with regard to gas-phlegmons, that the formation of gas is a secondary process, but admits, of course, that this process may take place during the life, not of the tissue, but of the individual. It is not quite clear why this possibility should be considered excluded in the case of inner organs. In the case here referred to it could not be determined whether the process has been ante- or post-mortem, but it seems probable that the gas-producer has been a secondary invader, perhaps an aerobic organism, since the anaerobic culture produced a diffuse phlegmon without any formation of gas.

XIX. MALARIA

In an earlier paper (1912, 2) I mentioned that, out of 69 cases of malaria, *P. vivax* was found in 9, *P. malariae* in 2, *P. praecox* in 37, *P. vivax* and *P. praecox* together in 2, and *P. malariae* and *P. praecox* together in 1 case; in 18 the result had not been stated.

This time the results were somewhat different: of 138 cases, which I examined together with Dr. Hernandez, 80 were infections with *P. vivax*, 10 with *P. malariae*, and 42 with *P. praecox;* 4 were mixed infections with *P. vivax* and *P. praecox*, and in 2 the species was not determined.

The total number of malarial cases admitted to hospital and lazaret had considerably increased, the increase depending chiefly on a larger number of tertian infections. Two circumstances may have contributed to this increase, namely the actual occurrence of more cases and, that more cases were sent from the country districts to be treated in Mérida. That more cases occurred than usual, was the opinion of practitioners working in different parts of the Peninsula; the reason is to be sought, probably, in the exceptional frequency of rainfalls during the late autumn and winter months, which are, ordinarily, very dry. Mosquitos were, as a consequence, fairly numerous even in January and in February, in which months I have in other years observed that they have been quite scarce. On the other hand, there is no doubt, that more malarial cases are now sent to the hospital in Mérida for treatment than in earlier times; this modern hospital has been in existence for a number of years, and landowners in remote parts, not only of Yucatán, but also of Campeche, are availing themselves of the opportunity thus afforded for having their labourers treated under better hygienic conditions than it is possible on most haciendas. A particularly large number of malarial cases came from Champotón, in the south-western part of Campeche, which seems to be the most severely infected part of the Peninsula.

A few attempts were made to determine the frequency of malaria in various places, which I visited with Dr. Casares with the object of making inquiries concerning yellow fever. Enlargement of the spleen-dulness was found in 31 of 143 school children examined in Temax, and in 15 of 119 in Motul, but in a few cases only the organ reached the curvature of the ribs and could be demonstrated by palpation. Malarial parasites were found in one case only from Temax, and in four from Motul. In one of the latter cases a single small ring was observed, and in all other cases except one, parasites were scarce (in two cases *vivax* and in one case *praecox*). In the remaining case, a child without febrile symptoms, apparently, numerous parasites (both *vivax* and *praecox*) were present.

There was a conspicuous lack of correspondence between the types of malarial fevers and the species of parasite found, not only in the infections with *P. praecox*, but also in those with *P. vivax* and *P. malariae*. In several cases of intermittent fevers with very high temperatures, *P. vivax* was very scarce, and, on the other hand, two cases were seen, in which very insignificant or no symptoms at all were observed, although parasites were numerous. Both were cases of mixed infections with *P. vivax* and *P. praecox*; in the one, just referred to, no temperature was taken, but the child went to school, and was apparently well. The other, in which the blood was swarming with parasites, was that of a young Spaniard, who had lived in a severely infected district (Champotón) for several months, and complained of slight headache and uneasiness, but knew nothing of fever;

when seen in hospital, at the time of the blood examination, his temperature was but slightly elevated, between 37° and 37·5° C.

The morphological characters of the parasites were those commonly observed; only in one case was the following peculiarity noticed. The parasites in this case were comparatively small, with the characters of *P. malariae* (especially transverse forms), but a few schizonts were seen dividing into a larger number of merozoites (text fig. VIII) than is characteristic of this species. According to the number of merozoites, the parasite in this case might be classified as *P. praecox*, or a mixed infection might exist, but the advanced stages of schizogony are in praecox infections, as a rule, not seen in the peripheral blood. Opinion on this point is still divided; without referring to earlier discussions, it may be mentioned, that Ziemann (1906) has observed division forms in praecox infections, in peripheral blood, in Italy, but not in West Africa; Marchoux (1911) says that they are not seen; and Ruge (1912) states that they are generally absent, but may occur, exceptionally, in very severe infections. In Yucatán I have seen adult schizonts in no other case of praecox infection.

Text Fig. VIII.

XX. INCLUSIONS IN LEUCOCYTES IN CASE OF LEG ULCER

Several cases of leg-ulcers were examined. *Leishmania tropica* was found in one case only, in which the patient suffered from ear-ulcer also. In other cases mixed bacterial infections were seen.

In one case I found some curious inclusions in a number of leucoytes, which shall now be described. The patient was a middle-aged Mexican woman, who had lived for several months in Champotón. She said that she had suffered very much from insect bites on the legs, and ascribed the ulcer to this cause. The ulcer was extensive, irregular, with granulating surface. Examination of smears showed the presence of numerous cocci and bacteria, but absence of *Leishmania*, spirochaetes and fusiform bacteria. In several leucocytes (mostly of the 'transitional' type) oval bodies were seen, which were sharply defined, with a kind of capsule or membrane, apparently thickened at both extremities. The bodies, when well characterized, possessed a large nucleus, of a shape corresponding to that of the body, and occupying its central portion, thus leaving a border of homogeneous protoplasm all round (Plate III, fig. 6). Similar bodies were also seen free in the smear (Plate III, fig. 8), but it is impossible to say, whether they have been so in vivo, or have escaped from ruptured cells at the preparation of the smear. In other cells smaller elements were observed, which would appear to represent remains of nuclei of the larger bodies (Plate III, fig. 7). It is difficult to discuss the nature of these inclusions, which were observed in no other case, though carefully looked for, especially in the case of another woman suffering from a similar ulcer, and having arrived from Champotón and been admitted to the hospital at the same time. They may be remnants of phagocytosed cells, though it is difficult to see what kind of cells they might represent. They may, on the other hand, be organisms, probably protozoa, in which case the question presents itself, whether they are harmless, casual parasites which have become phagocytosed, after having settled on the already developed ulcer, or whether they are of pathogenic importance. They are somewhat similar to the parasites which have been found in leucocytes and described under the name of *Leucocytogregarina* by Porter (1909).

XXI. HAEMATOLOGICAL REMARKS

During the numerous careful examinations of blood films, when searching for parasites, I had abundant opportunity of studying blood platelets in their different forms. They showed extreme variations, in size and morphological characters, both in human blood (Plate III, figs. 32-39), and in blood of several mammals examined, particularly in that of cattle (Plate III, figs. 40-46).

The origin of blood platelets has been a much debated question as long as these elements have been known. With regard to the opinions of earlier authors, I must refer to works on haematology; I will only mention that Schilling (1912, 1 and 2) from his recent observations has drawn the conclusion that the platelet represents the nucleus of the erythrocyte. Some of my observations (Plate III, figs. 32, 33 and 34) would appear to support this view, as the platelets shown in these figures might well be either intracorpuscular, or in the act of escaping from the erythrocyte. But platelets as large as, or even larger than, erythrocytes (figs. 36, 37 and 38 from human blood, figs. 42 and 45 from cattle) cannot be explained in the same way. It is obvious that, should such large and well-defined bodies have taken their origin from other cells, as expelled nuclei or in a similar way, we should have to seek their mother cells amongst much larger cells than the erythrocytes. Mononuclear leucocytes might be thought of, but I have seen nothing which might suggest the existence of such a connection. A twofold origin of the platelets might be thought of, but it appears more probable that these elements are essentially different from both erythrocytes and leucocytes, thus corresponding to the nucleated thrombocytes of lower animals. They seem to have a function similar to that of the last mentioned bodies, and the morphological characters are not wholly unlike. The protoplasm in both stains very faintly and seems completely different from that of both leucocytes and erythrocytes. A well defined, and strongly stained, borderline, which is common in thrombocytes, is also seen in some platelets (figs. 37 and 39). The nuclear structures are, of course, essentially different: in thrombocytes well defined nuclei, and in platelets loose, irregularly distributed masses which show some resemblance to chromatin. At any rate, an independent origin seems more probable than the evolution which Schilling describes; according to the former view it seems natural, that small, irregularly shaped platelets may be remainders of large and well defined, whilst, on the other hand, expelled erythrocyte nuclei could not be supposed to develop and attain much larger dimensions than they originally possessed. The relationship which one believes one may see in figures as those above referred to, would be apparent only, depending on adhesion of platelets to erythrocytes.

In a few cases 'corps en demi-lune' were seen; these bodies evidently are transformed erythrocytes, but the actual process of their formation is unknown.

XXII. TECHNICAL REMARKS

Giemsa (1910, 2) has recently modified his staining method in such a way that it can be used as a 'quick method.' This is an advance of very great importance in practical work. It appeared to me very doubtful, whether this method could be applied to the staining of *P. flavigenum*, as a prolonged action of the solution had been found necessary in order to obtain good results by the ordinary technique. Fortunately, however, good results were obtained, when the action of the undiluted solution was prolonged to one minute, and of the diluted to ten, but otherwise Giemsa's technique scrupulously adhered to. Special stress should be laid upon keeping the slide covered during the action of the undiluted solution, and upon rapid and careful mixing of the solution with distilled water without shaking. I have also found it of even greater importance in this than in other Giemsa methods that the distilled water should be of absolutely neutral reaction. Some care should be taken, when washing the film, after staining, as it may decolourize by a prolonged exposure to a strong current of tap water. The only difference, which I have noticed, is that films, stained according to this technique, often, but not always, fade somewhat more quickly than those treated by the slow method.

Three different stock solutions were used: Giemsa's solution (Grübler), old, and new formula, and Pappenheim's Panchrom for smears (Grübler). All gave equally good results on all kinds of blood examined, when used according to the 'slow Giemsa method,' but in their application as 'quick methods' a noteworthy difference was observed, when working with blood of snakes. All blood elements and parasites (haemogregarines) observed in this blood stained well with Giemsa's solution, old formula, quick method, but not so with the two other solutions. In the latter case haemogregarines, and erythrocyte-nuclei stained very badly, but the nuclei of leucocytes and thrombocytes fairly well.

For sections Giemsa's solution, old formula, and panchrom for sections, were employed according to the acetone technique (Giemsa, 1910, 1, and Seidelin, 1911, 6); both gave equally good results.

The iron-haematein technique (Seidelin, 1911, 6) gave good results, not only on sections and wet films, as previously recommended, but also, in many cases, on dried smears fixed in methyl alcohol. The nuclear staining is, with this method, often less intense than that obtained with Heidenhain's stain, but the nuclear structures stand out very well defined, and it has always the great advantage

Text Fig. IX.

that no differentiation is used, an advantage which not only gives it a wider scope of application but also assures more reliable results. The sharp definition of the chromatin in *P. flavigenum* is illustrated in the accompanying figures (text fig. IX, *a* and *b*).

XXIII. SUMMARY

P. flavigenum was found in practically all cases of yellow fever, in a number of suspicious cases, and in two apparently healthy native children; it was not found in other febrile diseases. I, therefore, consider it the pathogenic parasite of yellow fever.

Yellow fever is endemic in Yucatán and, probably, in Campeche and in Quintana Roo. It attacks natives, generally as children and in mild, atypical forms, but occasionally also in severe, even fatal forms, typical or atypical. Cases in foreigners are often severe.

An ulcerative affection of the ear, produced by *Leishmania tropica*, is of common occurrence.

Infections with *Babesia bigemina* and with a bacterium similar to, if not identical with, *Bacterium anthracis* are frequent in cattle.

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APPENDIX

LIST OF CASES WHICH WERE CONFIRMED BY THE HEALTH AUTHORITIES OF MERIDA

Name	Residence	Nationality	Age	Length of residence	Entered Lazaret	Diagnosis confirmed	Result
1. J. B. ...	Carcel de Mujeres ...	Guadalajara	22 years	4 months	Aug. 3	Aug. 6	Recovery 14 Aug., 1911
2. R. O. ...	Carcel de Mujeres ...	Atumba—Durango	30 ,,	8 ,,	,, 1	,, 6	Recovery 18 Aug., 1911
3. O. P. ...	Carcel de Mujeres ...	Tlascala	21 ,,	8 ,,	,, 18	,, 24	Death 24 Aug., 1911
4. S. M. ...	Carcel de Mujeres ...	Puebla	26 ,,	8 ,,	,, 23	,, 28	Death 29 Aug., 1911
5. A. P. ...	Carcel de Mujeres ...	Puebla	27 ,,	5 ,,	,, 23	,, 29	Recovery 6 Sept., 1911
6. L. C. ...	Carcel de Mujeres ...	Puebla	26 ,,	8 ,,	,, 23	,, 29	Death 30 Aug., 1911
7. R. R. ...	Carcel de Mujeres ...	Guanajuato	30 ,,	10 ,,	,, 25	,, 29	Death 31 Aug., 1911
8. M. T. ...	Carcel de Mujeres ...	Tlascala	22 ,,	8 ,,	,, 6	,, 29	Death 1 Sept., 1911
9. P. R. ...	Carcel de Mujeres ...	Puebla	27 ,,	5 ,,	,, 29	,, 30	Recovery 9 Sept., 1911
10. G. R. ...	Cuartel de Dragones	Ocoyoac—México ...	26 ,,	2 ,,	,, 28	,, 31	Recovery 9 Sept., 1911
11. N. A. ...	Cuartel de Dragones	Hidalgo	27 ,,	2 ,,	,, 27	,, 31	Recovery 6 Sept., 1911
12. P. M. ...	Calle 61 número 425	Guanajuato	30 ,,	2 ,,	Sept. 4	Sept. 8	Recovery 18 Sept., 1911
13. M. H. ...	Calle 61 número 431	Tatepex—México ...	14 ,,	2 ,,	,, 5	,, 8	Recovery 16 Sept., 1911
14. T. T. ...	Carcel de Mujeres ...	Tlascala	21 ,,	8 ,,	,, 7	,, 11	Death 15 Sept., 1911
15. J. M. ...	Cuartel de Dragones	Hidalgo	22 ,,	2 ,,	,, 8	,, 13	Recovery 18 Sept., 1911
16. J. G. ...	Carcel de Mujeres ...	Michoacan	38 ,,	8 ,,	,, 10	,, 13	Recovery 21 Sept., 1911

Name	Residence	Nationality	Age	Length of residence	Entered Lazaret	Diagnosis confirmed	Result
17. L. G.	Carcel de Mujeres	Teleta—México	22 years	6 months	Sept. 10	Sept. 15	Recovery 21 Sept., 1911
18. A. V.	Calle 55 núm. 444	Veracruz	9 ,,	2 ,,	,, 13	,, 15	Death 15 Sept., 1911
19. G. P.	Carcel de Mujeres	Guanajuato	40 ,,	6 ,,	,, 11	,, 16	Recovery 25 Sept., 1911
20. M. P. R.	Calle 61 número 425	Michoacan	38 ,,	2 ,,	,, 13	,, 16	Recovery 23 Sept., 1911
21. F. A.	Carcel de Mujeres	Michoacan	30 ,,	6 ,,	,, 11	,, 18	Recovery 22 Sept., 1911
22. A. M.	Carcel de Mujeres	Puebla	32 ,,	2 ,,	,, 13	,, 18	Death 20 Sept., 1911
23. G. P.	Calle 44 número 508	Guanajueta	11 ,,	3 ,,	,, 17	,, 17	Death 18 Sept., 1911
24. M. S.	Cuartel de Dragones	Oaxaca	45 ,,	2 ,,	,, 16	,, 18	Recovery 27 Sept., 1911
25. A. G.	Carcel de Mujeres	San Luis Potosi	26 ,,	8 ,,	,, 13	,, 18	Recovery 22 Sept., 1911
26. L. F.	Carcel de Mujeres	Puebla	30 ,,	10 ,,	,, 19	,, 22	Death 24 Sept., 1911
27. M. C. T.	Calle 48 número 502	Puebla	18 ,,	2 ,,	,, 19	,, 22	Recovery 2 (?) Sept., 1911
28. E. M.	Carcel de Mujeres	San Luis Potosi	27 ,,	10 ,,	,, 20	,, 23	Death 25 Sept., 1911
29. E. S.	Calle 39 número 414	Nuevo Léon	26 ,,	2 ,,	,, 20	,, 25	Recovery 27 Sept., 1911
30. J. C.	Calle 61 número 431	México (D.F.)	25 ,,	2 ,,	,, 20	,, 26	Recovery 4 Oct., 1911
31. M. S.	Cuartel de Dragones	Guerrero	26 ,,	3 ,,	,, 20	Oct. 2	Recovery 16 Oct., 1911
32. A. L.	Carcel de Mujeres	Puebla	28 ,,	11 ,,	Oct. 1	,, 4	Death 6 Oct., 1911
33. P. G.	Carcel de Mujeres	Puebla	27 ,,	7 ,,	,, 5	,, 9	Death 11 Oct., 1911

Name	Residence	Nationality	Age	Length of residence	Entered Lazaret	Diagnosis confirmed	Result
34. T. V. ...	Carcel de Mujeres ...	México (D.F.) ...	30 years	7 months	Oct. 10	Oct. 13	Recovery 20 Oct., 1911
35. M. C. ...	Calle 59 número 435	Hidalgo	23 ,,	3 ,,	,, 9	,, 13	Death 17 Oct., 1911
36. M. C. C.	Calle 61 número 425	Veracruz	18 ,,	3 ,,	,, 9	,, 16	Recovery 20 Oct., 1911
37. A. G. ...	Cuartel de Dragones	Veracruz	25 ,,	3 ,,	,, 21	,, 26	Recovery 31 Oct., 1911
38. M. D. ...	Calles 70 y 75 ...	Guanajuato	21 ,,	18 ,,	,, 23	,, 26	Death 30 Oct., 1911
39. D. O. ...	Cuartel de Dragones	Toluca	29 ,,	3 ,,	,, 14	,, 26	Death 28 Oct., 1911
40. T. V. ...	Cuartel de Dragones	Puebla	25 ,,	3 ,,	,, 21	,, 28	Death 30 Oct., 1911
41. E. M. ...	Calle 57 número 470	España	19 ,,	10 ,,	,, 28	,, 28	Death 28 Oct., 1911
42. J. V. ...	Calles 70 y 75 ...	Sonora	20 ,,	3 ,,	,, 26	,, 30	Death 31 Oct., 1911
43. C. V. ...	Cuartel de Dragones	Hidalgo	20 ,,	3 ,,	,, 27	,, 31	Death 2 Nov., 1911
44. M. R. G.	Calle 46 número 481	San Luis Potosí ...	23 ,,	3 ,,	Nov. 7	Nov. 11	Death 13 Nov., 1911
45. J. T. S. ...	Calle 50 número 508	Turquia	18 ,,	(?) ..	,, 11	,, 12	Death 15 Nov., 1911
46. A. A. ...	Calle 69 número 608	México (D.F.) ...	22 ,,	1 ,,	,, 15	,, 16	Death 17 Nov., 1911
47. J. C. ...	Calle 61 número 431	Oaxaca	24 ,,	8 years	,, 15	,, 16	Death 20 Nov., 1911
48. J. G. B.	Cuartel de Dragones	Manilance	30 ,,	5 months	Dec. 13	Dec. 15	Death 16 Dec., 1911
49. C. M. ...	Calle 50 número 453	Seul—Corea	36 ,,	7 years	,, 17	,, 19	Recovery 20 Dec., 1911
50. R. T. ...	Calle 55 número 444	México (D.F.) ...	22 ,,	6 months	,, 21	,, 23	Death 25 Dec., 1911

Name	Residence	Nationality	Age	Length of residence	Entered Lazaret	Diagnosis confirmed	Result
1. I. A. ...	Temax	Pachuca—México ...	20 years	10 days	Dec. 30	1912 Jan. 4	Recovery 8 Jan., 1912
2. F. O. ...	Temax	Jacona—México ...	27 ,,	2 months	1912 Jan. 2	,, 4	Death 5 Jan., 1912
3. M. G. ...	Maxcanú	México (D.F.) ...	22 ,,	1 year	Cured in Maxcanú	,, 7	Recovery 9 Jan., 1912
4. F. S. ...	Puerto ‘ San Felipe ’	Guadalajara	26 ,,	28 days	Jan. 10	,, 14	Recovery 18 Feb., 1912
5. E. P. D....	Calle 60 número 342	Francia	32 ,,	2 months	—	,, 17	Recovery 18 Feb., 1912
6. S. C. ...	Hacienda Kambul ...	Yucateco	31 ,,	—	Jan. 26	,, 27	Death 27 Jan., 1912
7. J. G. ...	Cuartel Dragones ...	Veracruz	25 ,,	7 months	,, 25	,, 29	Recovery 30 Jan., 1912
8. J. R. P. ...	Hacienda Kambul ...	Yucateco	30 ,,	—	,, 27	,, 30	Recovery 1 Feb., 1912
9. P. A. ...	Hacienda Kambul ...	Yucateco	32 ,,	—	,, 27	,, 30	Recovery 1 Feb., 1912
10. P. M. G.	Calle 55 número 444	México (D.F.) ...	33 ,,	7 months	,, 30	,, 31	Death 31 Jan., 1912
11. O. R. ...	Cuartel Dragones ...	Queretaro	35 ,,	7 ,,	Feb. 8	Feb. 10	Recovery 21 Feb., 1912
12. L. P. ...	Cuartel Dragones ...	Oaxaca	26 ,,	7 ,,	,, 8	,, 10	Recovery 15 Feb., 1912
13. P. T. ...	Calle 69 número 328	México	64 ,,	7 ,,	,, 21	,, 23	Death 4 Mar., 1912
14. A. D. ...	Hotel Suizo	I. Canarias (Espa.) ...	21 ,,	7 years	Mar. 17	Mar. 18	Recovery 30 Mar., 1912
15. L. M. ...	Ex-Ciudadela S. Benito	Hermosillo Sonora ...	32 ,,	4 ,,	,, 17	,, 21	Recovery 21 Mar., 1912
16. J. L. ...	Calle 67 número 462	México (D.F.) ...	42 ,,	1 month	April 30	May 1	Death 2 May, 1912

Name	Residence	Nationality	Age	Onset of Disease	Result
1. P. C. ...	Hacienda Kambul ...	Yucateco	25 years	Dec. 14, 1911	Death on 6th day of disease
2. F. C. ...	Hacienda Kambul ...	Yucateco	10 ,,	,, 17 ,,	,, 8th ,, ,,
3. P. B. ...	Hacienda Kambul ...	Yucateco	40 ,,	,, 30 ,,	,, 8th ,, ,,
4. H. C. ...	Hacienda Kambul ...	Yucateco	35 ,,	,, 18 ,,	,, 8th ,, ,,
5. S. B. ...	Hacienda Kambul ...	Yucateco	—	,, 11 ,,	,, 10th ,, ,,
6. J. T. ...	Hacienda Kambul ...	Yucateco	—	Jan. 3, 1912	,, 8th ,, ,,
7. M. C. ...	Hacienda Kambul ...	Yucateco	—	,, 18 ,,	,, 9th ,, ,,

PROPOSAL BY DR. CASARES, DELEGATE OF THE SUPERIOR BOARD OF HEALTH

In this Proposal the City of Mérida, for the purpose of sanitary administration, is divided by Dr. Casares into four districts as follows:—

The first district is split up into four divisions.

Content	First division	Second division	Third division	Fourth division
Dwelling houses of immunes	394	856	869	757
Dwelling houses of non-immunes	57	69	71	40
Non-immune individuals ...	143	344	202	73
Water storage tanks	115	208	234	90
Wells	92	149	155	109
Rain-water cisterns	37	52	60	6
Cesspools	104	267	168	2
Water closets	118	186	130	0
Cesspool ventilators	48	80	129	1

This district is visited by four sanitary inspectors, each inspector having charge of one division, and, each visiting on an average fifteen houses per day, the whole round occupying 26 days for the first, 60 days for the second, 62 days for the third, and 50 days for the fourth division.

The second district is split up into five divisions, although hitherto there have only been four, the new division being formed provisionally on account of the principal focus in the military quarters situated in this district.

Content	First division	Second division	Third division	Fourth division	Fifth division
Dwelling houses of immunes	674	329	252	880	926
Dwelling houses of non-immunes	138	40	31	51	70
Non-immune individuals	457	137	87	158	187
Water storage tanks ...	309	47	72	297	180
Wells	250	47	49	211	161
Rain-water cisterns ...	127	11	5	56	38
Cesspools	448	26	14	158	104
Water closets	510	16	11	150	107
Cesspool ventilators ...	438	19	12	240	41

This district is visited by five sanitary inspectors, each inspector having charge of one division, and, each visiting on an average fifteen houses per day, the whole round occupies 45 days for the first, 21 days for the second, 17 days for the third, 59 days for the fourth, and 62 days for the fifth division.

The third district is split up into four divisions.

Content	First division	Second division	Third division	Fourth division
Dwelling houses of immunes	824	803	1173	406
Dwelling houses of non-immunes	47	54	87	99
Non-immune individuals ...	152	158	450	270
Water storage tanks	356	276	243	162
Wells	249	167	228	158
Rain-water cisterns	110	67	36	24
Cesspools	385	188	69	34
Water closets	366	176	66	74
Cesspool ventilators	305	173	86	33

This district is visited by four sanitary inspectors, each visiting on an average fifteen houses per day, and the whole round occupies 55 days for the first, 54 for the second, 78 for the third, and 27 for the fourth division.

The fourth district is split up into four divisions.

Content	First division	Second division	Third division	Fourth division
Dwelling houses of immunes	608	637	771	1038
Dwelling houses of non-immunes	136	56	94	92
Non-immune individuals ...	287	117	212	192
Water storage tanks	296	310	259	219
Wells	165	178	189	197
Rain-water cisterns	88	88	61	62
Cesspools	454	320	176	225
Water closets	395	349	181	166
Cesspool ventilators	384	394	154	100

This district is visited by four sanitary inspectors, each visiting on an average fifteen houses per day, and the whole round occupies 40 days for the first, 42 days for the second, 52 days for the third, and 69 days for the fourth division.

MERIDA, *January*, 1912.

According to this proposal a new plan of campaign was submitted to the Mexican Congress by Dr. E. Licéaga, President of the Superior Board of Health, and approved.

NEW PLAN OF CAMPAIGN AGAINST YELLOW FEVER IN YUCATÁN

BY E. LICÉAGA

In spite of the precautions taken in Mérida, an epidemic broke out in August last year, and has lasted up to the time author wrote this paper, i.e., February 23rd, 1912. Yet this epidemic has shown a general reluctance in spreading, only 65 cases with 29 deaths having occurred up till then. These cases were very unequally distributed over the seven months, and only during the last month had the disease spread to any distance outside the City of Mérida. It is argued that, supposing the measures effectively employed in México, as well as in other countries, had in this instance failed to work, some special factor must have played a part in the reappearance of yellow fever in Mérida.

Medical men of Cuba and Yucatán, as well as those who have studied the question in Africa, maintain that infection is kept up by atypical cases in the adult, but especially by those in the child. In this case it would not be sufficient, in order to prevent an epidemic, to isolate yellow fever patients only, as all those who are affected with atypical or larval forms of the disease will thus remain unprotected, owing to the want of any infallible diagnostic means for the detection of such atypical cases.

If it is impossible to secure the isolation of all, on account of the unrecognized atypical cases, then isolation as the means of disconnecting the three factors necessary for the dissemination of yellow fever is insufficient, and it will become necessary to pay more attention to the other two factors, viz., mosquito-destruction and protection of non-immunes.

As the efficient protection of all non-immunes proved impracticable, recourse was taken to the radical destruction of mosquitos. This was practised with the method employed by Colonel Gorgas in Cuba, but improved in accordance with the experience gained by the Sanitary Authorities of the Panama Canal Zone.

For the purpose of the Campaign, the City of Mérida is to be divided into five districts with eight sub-divisions each, except the fifth district which will only have three. The staff of sanitary inspectors is to be increased to ensure proper attention.

This arrangement was proposed with the object of drawing up a register of all non-immunes residing in the City, and to have them visited daily. If they show any rise in temperature, they are to be regarded as suspicious and isolated to protect them from the bites of mosquitos. This isolation is to be performed in a carefully screened lazaret.

The sanitary inspectors visiting the non-immunes will also examine all collections of water in and about the house, and immediately take the necessary steps if larvae are present. All receptacles containing water used for domestic purposes, which cannot be covered in the manner approved, must be covered by a thin layer of petroleum, and, if necessary, a cock provided at the lower part of the receptacle to allow water to be obtained without disturbing the protecting layer of petroleum.

The sanitary inspectors have further to see to the petrolization of all other collections of water of any description; no such collection is to be left uncovered.

It is thought advisable to find out whether the Millions, or a similar species, are represented in Mérida, so as to propagate them for the destruction of larvae. The medical practitioner should urge that the rain-water drains are sufficiently on the incline, so that no water can remain stagnant in the drains.

The formation of leagues is recommended to assist in the fight against yellow fever and malaria in all localities of any importance, and to urge the authorities of the State of Yucatán to issue a bye-law which will compel all inhabitants to keep water used for domestic purposes free from larvae, in order to minimize the possibilities of being bitten by mosquitos and the consequent dangers to which they otherwise would be exposed.

EXPLANATION OF PLATES

The figures have been drawn with Abbe's camera lucida, using Zeiss's apochr. imm. 3 mm. and compens. oc. 12. The magnification varies from 1,400 to 1,550 lin., according to the height of the drawing table. All figures are drawn from specimens stained with Giemsa's solution or with Pappenheim's 'panchrom.'

PLATE I

Figs. 1-5.—Different forms of *Paraplasma flavigenum* from case A.D., on first or second day of recrudescence.

Figs. 6-10.—Small ring-forms. In fig. 7 a blood platelet is shown, lying close to the parasite, either in or upon the erythrocyte.

Figs. 11-12.—Rod-shaped forms.

Figs. 16-19, and 21.—Dividing forms in peripheral blood.

Fig. 20.—Larger dividing form in smear from liver.

Figs. 22 and 23.—Marginal bodies; peripheral blood.

Figs. 24 and 25.—Larger forms with solid protoplasm; peripheral blood.

Figs. 26, 30, 31 and 32.—Free forms in peripheral blood.

Figs. 27-29.—Free forms in wall of stomach.

Figs. 33-37.—Parasite-like bodies in protoplasm of polymorphonuclear leucocytes and in monocytes.

Plate I

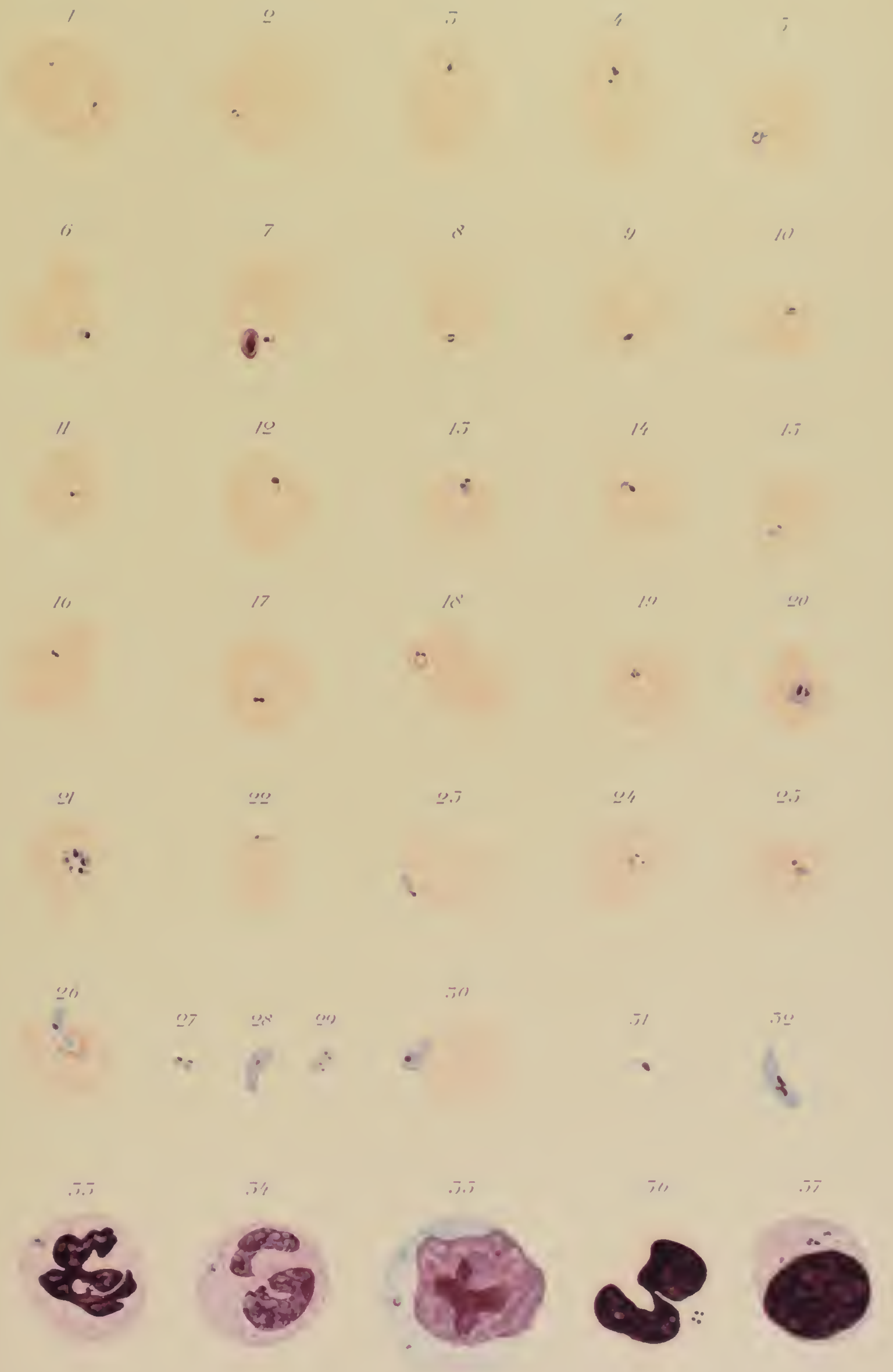

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PLATE II

Figs. 1-15.—Forms observed in the case H.S., 1-4 on the forenoon of the first day, 5-8 on the evening of the same day, 9-11 on the second day, and 12-15 on the sixth day.

Figs. 16-23.—Elements, apparently parasites, observed in the blood of guinea-pig inoculated with yellow fever blood, containing *P. flavigenum.*

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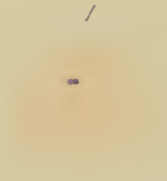

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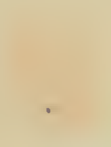

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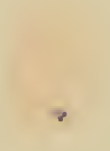

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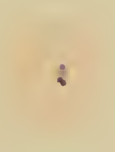

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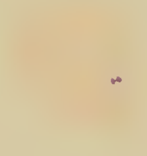

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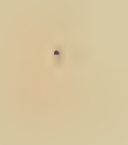

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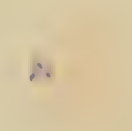

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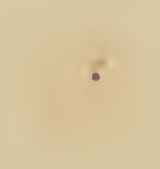

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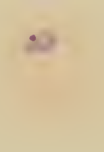

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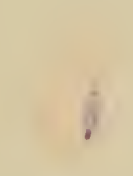

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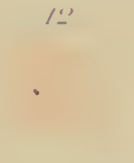

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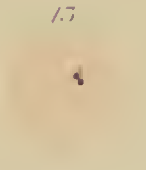

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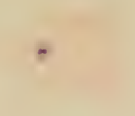

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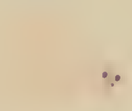

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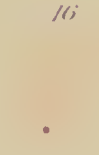

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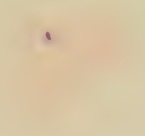

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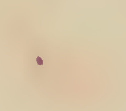

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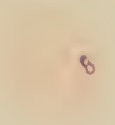

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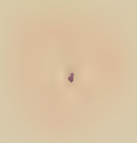

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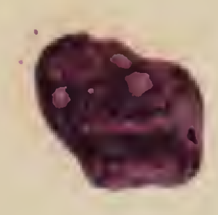

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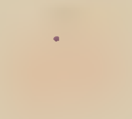

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PLATE III

Figs. 1 and 2.—*Leishmania tropica* in smears from ear-ulcer.

Figs. 3-5.—Diplococci in same specimens.

Figs. 6-8.—Bodies observed in smears from leg-ulcer.

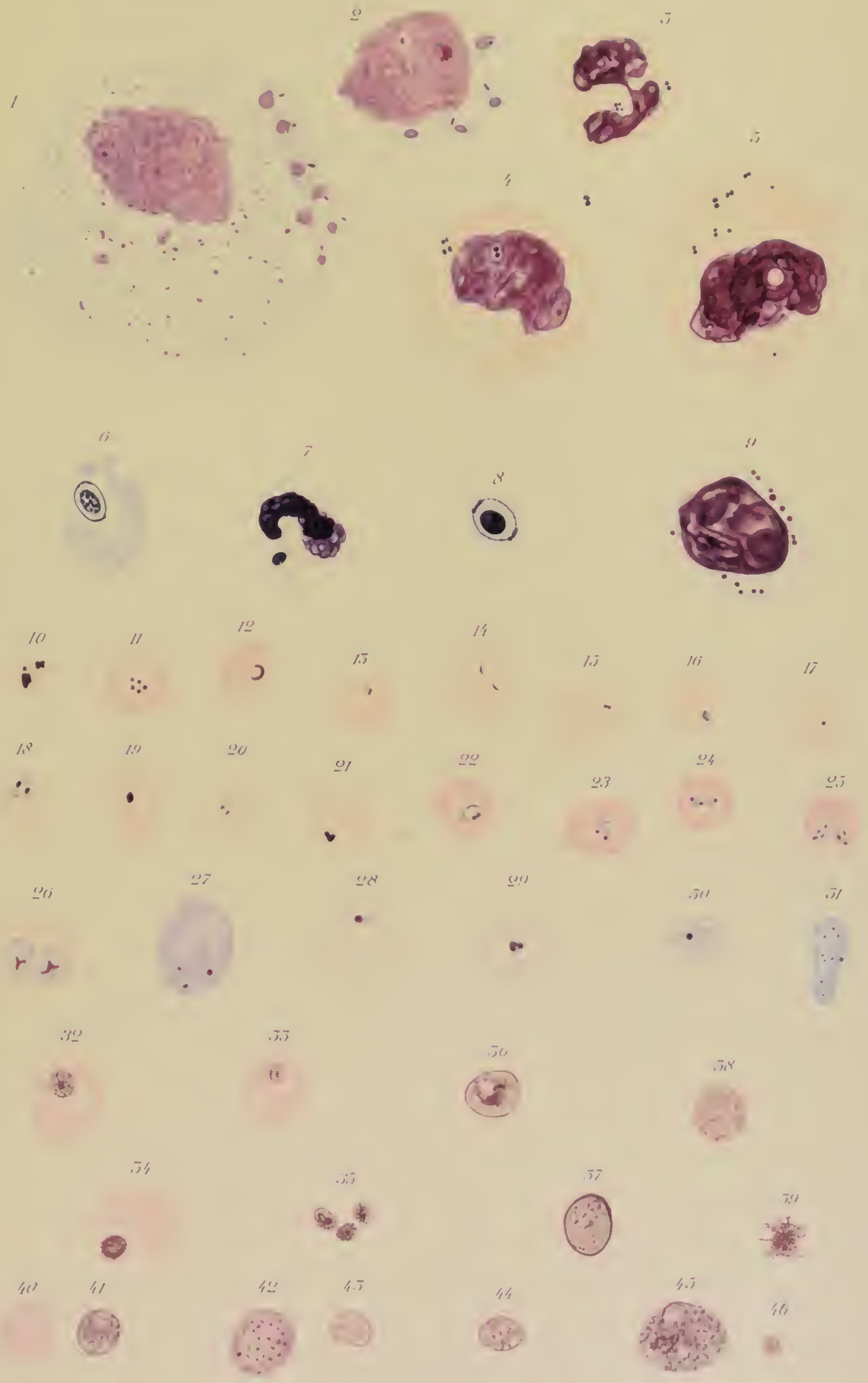
Fig. 9.—Monocyte with chromatin granules (remains of parasites?) from case of infection with *Babesia bigemina.*

Figs. 10-25.—*Babesia bigemina.*

Figs. 26-31.—*Babesia canis.*

Figs. 32-39.—Blood platelets from human blood.

Figs. 40-46.—Blood platelets from cow's blood.



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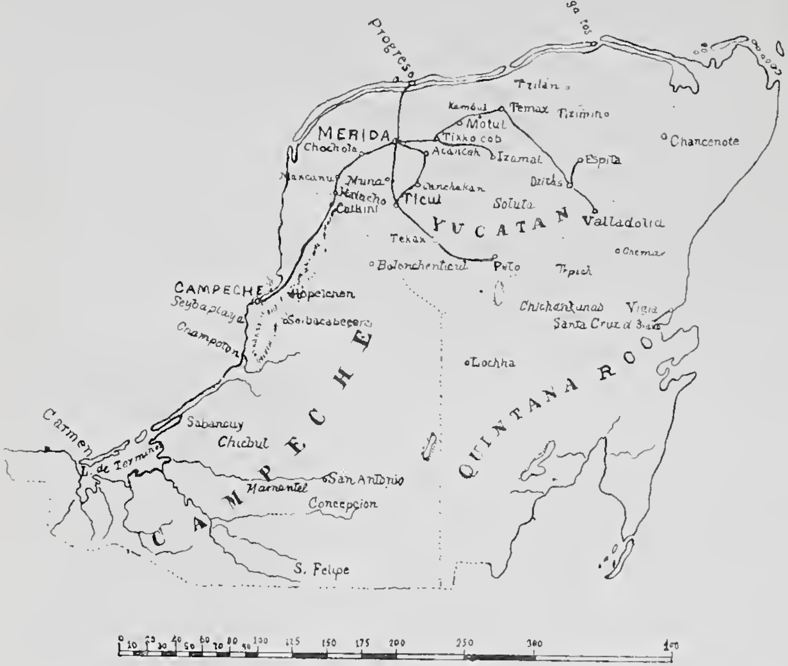

MAP OF YUCATÁN

MAP OF MERIDA: SHOWING MOSQUITO DISTRIBUTION

(*To illustrate section XIII*)

1. Palacio de Gobierno y Oficinas
2. Catedral
3. Palacio Legislativo
4. Jefatura Politica y Camandancia de Policia
5. Direccion Gral. del Registro Civil
6. Cementerio Gral.
7. Hospital O'Horan
8. Asilo Ayala
9. Asilo de Mendigos 'Celarin'
10. Penitenciaria 'Juarez'
11. Cárcel de Mujeres
12. Escuela Correccional de Artes y Oficios
13. Escuela Normal de Profesores
14. Instituto Literario de Estado
16. Cuartel de Cabelleria
17. Comisaria de San Sebastian
18. id. de Santiago
19. id. de Santana
20. Museo Yucateco
21. Escuela Central Municipal
22. Escuelas Municipales de niños y niñas del suburbio de Sn. Sebastian
23. Escuela Mpal. de niñas de Santiago
24. Rastro Público
25. Mercado Garcia Rejón
26. Nuevo Mercado
27. Pescaderia
28. Cuartel Federal
29. Seminario Conciliar
30. Colegio de Teresianas
31. Iglesia de Jesús Maria
32. id. id. Santiago
33. ,, ,, San Juan
34. ,, ,, San Cristobal
35. ,, ,, La Candelaria
36. ,, ,, Sta Lucia
37. ,, ,, La Ermita de Sta Isabel
38. ,, ,, Nitra Sra de Lourdes
39. ,, ,, Itzimma
41. San Pedro
42. Capilla del Sr. R. Quintero

Larvae or imagines of *S. fasciata* have been found in the blocks marked X. As a rule larvae were found in several houses of each block, in exceptional cases one only. The map represents only a minimum distribution of *S. fasciata*, as mosquitos have not been collected from all houses in which they have been observed. Places in which other mosquitos were found but not *S. fasciata*, have not been marked.

From the outskirts of the city and from the suburbs no data were available.